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Safety and effectiveness of endoscopic mucosal resection or endoscopic submucosal dissection for gastric neoplasia within 2 days' hospital stay

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Abstract

Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) have been well-established methods of treating upper gastrointestinal neoplasia. The aim of this study was to identify the safety and effectiveness of endoscopic treatment for gastric neoplasia within a 2-day hospital stay.

Between 2004 and 2015, a total of 914 patients with gastric neoplasia were treated with EMR or ESD within 2 days of hospitalization. The neoplasia sites, en bloc resection rates, pathology, local residual neoplasia rates, and major complications were evaluated retrospectively.

The mean age was 63.4 years old, and 636 (69.6%) patients were male. Adenoma was the most common final diagnosis (60.9%), followed by adenocarcinoma (28.9%). The first follow-up endoscopy was performed 4.9 ± 1.1 months after the procedure, and an average of 4.4 endoscopic examinations were performed for 7.16 years (range, 2.1 to 10.2 years). Additional surgery was performed in 11 (1.2%) cases based on post-procedure pathology results. On follow-up endoscopy, a mean of 5.9 months after the procedure, there were 18 residual neoplasia cases (EMR = 13, ESD = 5). Only 4 (0.4%) patients returned to the emergency unit with delayed bleeding, but all 4 cases were successfully controlled with endoscopic treatment. There were no other complications such as delayed perforation or aspiration pneumonia during the 2 days in hospital.

EMR and ESD within only 2 days in hospital showed safe and effective outcomes in terms of managing early gastric neoplasia with low complication and local residual rates.

Abbreviations: CP = clinical pathway, EMR = endoscopic mucosal resection, ESD = endoscopic mucosal dissection, IT = insulation-tipped.

Keywords: endoscopic mucosal resection, endoscopic submucosal dissection, length of stay

1. Introduction

Gastric cancer is the fourth most common cancer worldwide and the third leading cause of cancer-related deaths.[1] Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) have been well-established treatments for gastric cancer and precancerous lesions.

Both procedures have multiple advantages such as being minimally invasive, showing good curative effects, requiring shorter average hospitalization times, and allowing the normal physiological structure of the gastrointestinal tract to be retained.[2,3] However, endoscopic resection is associated with complications such as bleeding and perforation, and concern about complications is a major reason for extended hospital stays following these procedures. In addition, the hospital stay may be extended because of the need for additional treatment after pathology results are confirmed. In the case of ESD, recent data show an average of 5 to 8 days of hospitalization.[4] The extension of hospital stay is associated with a decrease in hospital profit, an increase in medical expenses, and hospital-acquired infections.[5,6] For this reason, many medical institutions are making efforts to reduce the number of hospital days.[6,7] Such efforts include sufficient pre-inspections at outpatient clinics and attempts to reduce complications associated with procedures.

From this background, the aim of this study is to investigate the safety and effectiveness of performing endoscopic resection for gastric neoplasm within 2 days in hospital.

2. Materials and methods

For this study, we enrolled patients who underwent EMR or ESD for premalignant lesions or early gastric cancer within 2 days at

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Seoul National University Bundang Hospital between January 2004 and April 2015. The patient was admitted after the EMR or ESD procedure on the scheduled date. If there was no complication until the day after the procedure, the patient was discharged before noon after a soft diet in the morning. There were no specific exclusion criteria related to gastric neoplasia.

Our institution has been conducting specific endoscopic treatment through Clinical Pathway (CP) since 2011; through CP, the process from hospitalization to treatment and discharge proceeds simply. We included all patients who received 1 of these endoscopic procedures through CP within 2 days.

We retrospectively evaluated all endoscopic findings before and after the EMR or ESD from the patient database. We analyzed the sites of lesions and pathology, margin involvement, complication rates, and residual neoplasia. Four experience endoscopists performed all of the endoscopic procedures.

During the procedures, midazolam (0.05–0.1 mg/kg) was used for sedation. All EMR and ESD procedures were performed with a standard single-channel endoscope (GIF-Q260, Olympus Optical Co, Ltd, Tokyo, Japan). In EMR, the procedure starts with injecting a mixture of normal saline and epinephrine into the submucosal space under the lesion to create a safety cushion; the cushion lifts the lesion, facilitating its capture and removal with a snare. In ESD, the typical sequences are marking with argon plasma coagulation, incision with an insulation-tipped knife (IT knife, KD-610L; Olympus), and submucosal dissection with simultaneous hemostasis. During EMR and ESD, we performed endoscopic hemostasis with the hemostatic forceps and hemoclip.

The study protocol was approved by the Institutional Review Board of SNUH (IRB No. B-1702-384-105).

2.1. Follow-up

Patients who received EMR or ESD were scheduled for follow-up endoscopy within the first 6 months after the procedure. If there is no residual tumor, follow-up is performed annually.

2.2. Definitions

We defined en bloc resection as resection of the neoplasia in 1 piece with no endoscopically residual neoplasia; we defined piecemeal resection as resection of neoplasia in multiple pieces.

We defined local residual neoplasia as when the endoscopist could detect the neoplasia at the primary resection site after follow-up EGDs (esophagogastroduodenoscopy) after curative endoscopic treatment of the primary lesion.

We defined bleeding as when a patient needed blood transfusion or endoscopic or surgical intervention because of hematemesis or melena or as a decrease in hemoglobin greater than 2 g/dL after the procedure.

We classified bleeding into 2 groups with respect to the time of onset: intra-procedure, which occurred during the endoscopic procedure, and postoperative, which occurred subsequent to the procedure. We diagnosed perforation when the endoscopist could directly observe the intra-abdominal space during the procedure or if free air was found on a plain chest X-ray after the procedure without a visible gastric wall defect noted during the procedure.

2.3. Statistical analysis

Data were analyzed by means of descriptive statistics (mean, standard deviation, or median, and range). Frequencies and percentages were calculated for categorical variables. All statistical tests were performed with the program, Statistical Package for the Social Sciences version 22.0 (SPSS).

3. Results

The clinicopathological characteristics of the patients who underwent curative EMR or ESD are shown in Table 1. From 2004 to 2015, a total of 3,221 patients underwent endoscopic treatment for upper gastrointestinal tract neoplasia, of whom 914 were treated within 2 days in the hospital; 340 (37.2%) of these patients were treated through CP.

Gastric neoplasms were located more frequently in the lower portion of the stomach (antrum, 674; low body, 121; mid-body, 53; high body, 50; cardia, 14; fundus, 3). We classified macroscopy types as protruded, flat elevated, flat, flat depressed, or excavated. Among these, the elevated type was most common (n = 588, 64.3%); there were also 88 protruding lesions (9.6%), 219 flat depressed lesions (24.0%), and 4 excavated lesions (0.4%). The median size of the primary neoplasia was 1.16 cm. Over half, 60.9% of patients (n=557) had tubular adenoma, and 28.9% (n = 264) had adenocarcinoma.

Endoscopic resection was performed using EMR in 459 patients (50.2%) and ESD in 455 patients (49.8%) and the rate of piecemeal resection was 3.8% (n=35). We performed the first follow-up endoscopy 4.9 ± 1.1 months after the procedure, and we performed an average of 4.4 endoscopic examinations for 7.16 (range, 2.1–10) years.

One hundred sixty-eight patients (18.4%) had tumor-positive lateral resection margins, 16 (1.8%) had tumor-positive deep resection margins, and 5 (0.5%) had uncheckable lateral resection margins. Of the patients with positive margins, 68.8% (n=121) underwent EMR and 31.2% (n=55) underwent ESD. We performed additional surgery in 11 cases based on post-

Table 1

Baseline characteristics of the 914 patients who had EMR or ESD within two days in the hospital.

	No. (%)
Age, yr	63.4
Sex	
Male	636 (69.6)
Female	278 (30.4)
Location of lesion	
Antrum	674 (73.7)
Low body	121 (13.2)
Mid body	53 (5.8)
High body	67 (7.3)
Pathology	
Tubular adenoma High grade	60 (6.6)
Low grade	497 (54.3)
Total	557 (60.9)
Tubular adenocarcinoma Well differentiated	194 (21.2)
Moderately differentiated	64 (7.0)
Poorly differentiated	6 (0.7)
Total	264 (28.9)
Gastritis	43 (4.7)
Hyperplastic polyp	21 (2.3)
Procedure	
EMR	459 (50.2)
ESD	455 (49.8)

EMR = endoscoic mucosal resection, ESD = endoscopic mucosal dissection.

Table 2

The characteristics of the 11 patients who had additional surgery after EMR or ESD.

No	Pathology (differentiation)	Margin involve		Depth	LN invasion	Op.	Days to Op. after EMR/ ESD
		Lateral	Deep				
1	Tubular adenocarcinoma (poor)	+	+	SM	–	TG	28
2	Tubular adenocarcinoma (poor)	–	–	SM	–	STG B-II	44
3	Tubular adenocarcinoma (well)	–	–	SM	+	STG B-I	55
4	Tubular adenocarcinoma (poor)	+	–	SM	–	STG B-I	35
5	Tubular adenocarcinoma (moderate)	+	–	MM	–	TG	41
6	Signet ring cell carcinoma	+	+	SM	–	STB B-II	40
7	Tubular adenocarcinoma (poor)	+	–	MM	–	STB B-II	47
8	Tubular adenocarcinoma (moderate)	–	+	SM	–	STB B-II	13
9	Tubular adenocarcinoma (moderate)	–	–	SM	+	STB B-II	31
10	Tubular adenocarcinoma (well)	–	–	SM	–	STB B-II	15
11	Tubular adenocarcinoma (moderate)	+	-	SM	+	STB B-II	25

EMR = endoscopic mucosal resection, ESD = endoscopic mucosal dissection, LN = lymph node, MM = muscularis mucosa, Op = operation, SM = submucosa, STG = subtotal gastrectomy, TG = total gastrectomy.

procedural histology, depth, margin involvement, and lymphatic invasion (Table 2). We considered additional surgery when the primary lesion was poorly differentiated or had tumor-positive deep resection margins or in cases of lymphatic invasion. We performed surgery an average of 34 days after the endoscopic procedure, with a range of 15 to 55 days.

Among the patients we included in our analyses, we detected neoplasia at the primary resection site during the first or second follow-up EGD within 12 months in 18 cases (1.9%); 13 of these 18 patients had previously undergone EMR, and 5 had undergone ESD (Fig. 1). After an additional ESD for the lesion that recurred, we saw no recurrence for a median of 49.2 months.

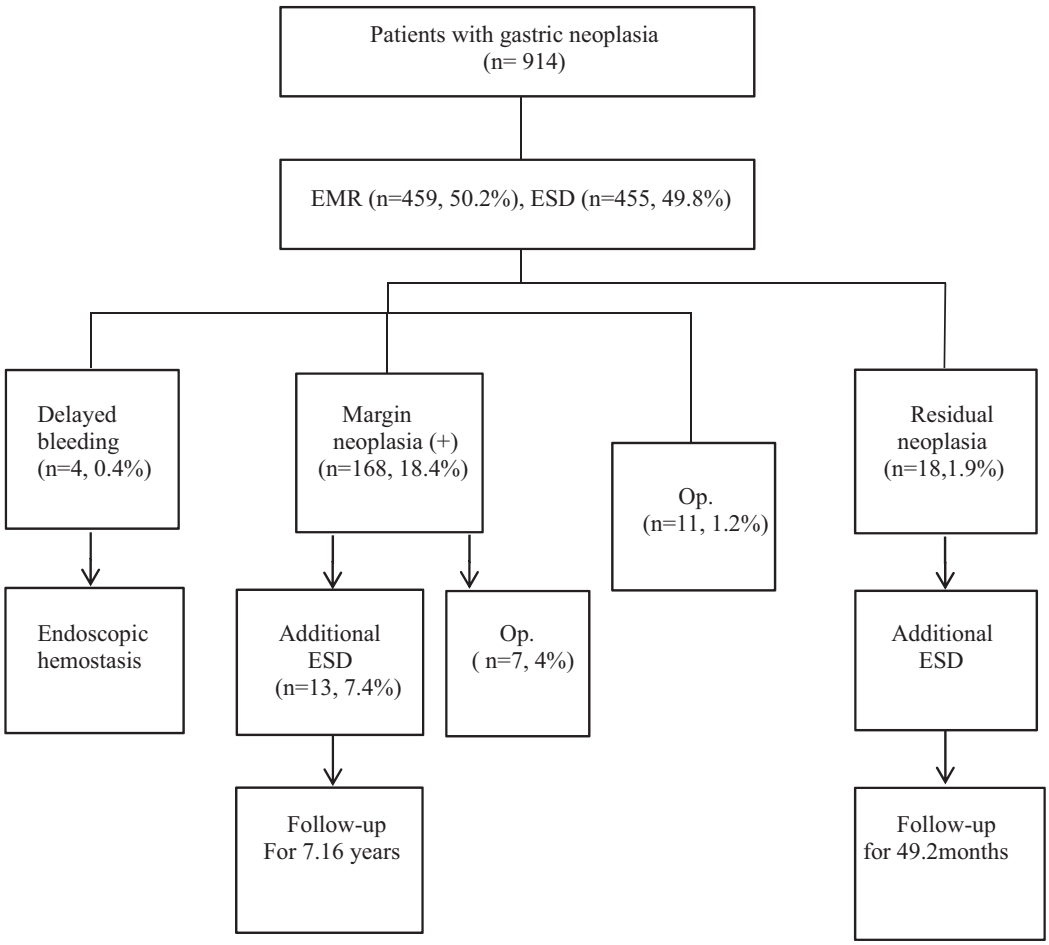

Figure 1. Flowchart of procedures. EMR = endoscopic mucosal resection, ESD = endoscopic submucosal dissection, Op = operation.

Table 3

Complications of the 914 patients who had EMR or ESD within 2 days in the hospital.

No.	Complication	Procedure	Sx	Date of visit after the discharge	Place of re-visit, Treatment
1	Oozing bleeding	EMR	Hematochezia	4	ER, Epinephrine injection Hemoclipping
2	Exposed vessel	ESD	Melena	9	ER, Epinephrine injection Hemoclipping Transfusion
3	Oozing bleeding	ESD	Melena	10	ER, APC Hemoclipping Transfusion
4	Ulcer bleeding	ESD	Hematochezia Hematemesis	1	ER, Hemoclipping Transfusion

APC = argon plasma coagulation, EMR = endoscopic mucosal resection, ESD = endoscopic mucosal disstection, Sx = symptom.

Post-procedure delayed bleeding occurred in 3 patients who underwent ESD and 1 who underwent EMR, and the patients returned to our emergency unit an average of 6 days after discharge (range, 1–10 days). Post-EMR bleeding showed an oozing appearance and was managed with endoscopic hemostasis; no patients needed transfusions following EMR but 3 post-ESD cases required transfusion after adequate hemostasis (Table 3).

Data on procedure-related perforation or aspiration pneumonia were not reported in this study.

The numbers of endoscopic treatments of gastric neoplasia performed every year at our hospital are shown in Figure 2 and the proportion of patients discharged after 2 days' hospital stay after the procedure without major complications is increasing.

4. Discussion

In this study, which analyzed EMR and ESD for a specific period, we found that delayed complication was rarely observed when the patient was discharged within two days after the procedure. We also confirmed that the patients who received additional treatment according to pathologic results were well managed without recur in long term follow up.

In Korea, endoscopic screening for gastric neoplasia is commonly performed; because of this, the detection rate of early gastric neoplasia is high, and these lesions are frequently treated using endoscopes. Periodic surveillance endoscopy simplifies identifying neoplasia recurrence, and as such, the endoscopic approach will gradually increase in the treatment of gastric neoplasia.[3] We have accumulated years of treatment experience with a variety of gastric neoplasia, and thus, we did not have to prolong the length of hospital stay unless there were special complications. Beginning in 2011, we performed endoscopic procedures using Clinical Pathway (CP), a multidisciplinary management tool based on evidence-based practice for specific groups of patients with predictable clinical courses.[8] CP aims for greater standardization of treatment regimens and sequencing as well as improved outcomes, from both quality of life and clinical outcomes perspectives.[8,9] We performed both EMR and ESD on the day the patient was admitted, and patients were discharged on the next day before noon, following a soft diet in the morning, if there were no complications. Once we introduced CP, the number of procedures we could complete within 2 days increased gradually. Most of the patients were treated through CP, but patients were excluded if there were any problems on the ward

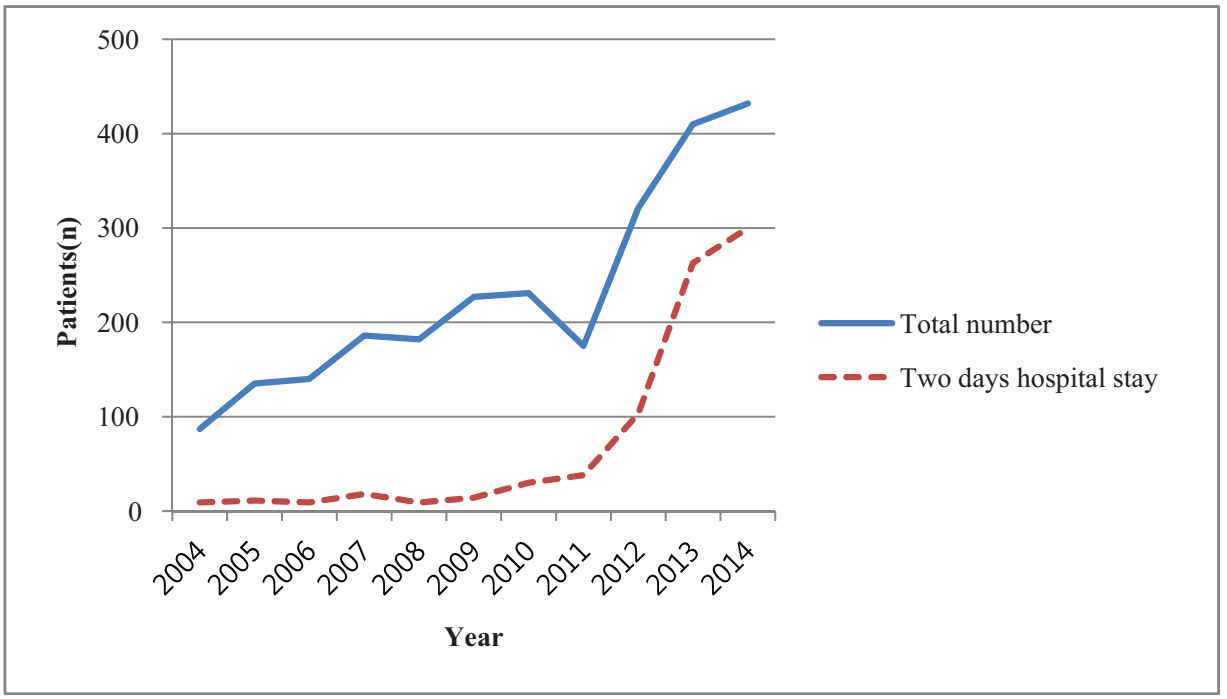

Figure 2. Annual number of patients who received EMR or ESD within 2 days in hospital. EMR = endoscopic mucosal resection, ESD = endoscopic submucosal dissection.

or if they needed any additional examinations during their hospitalization. In addition, we discontinued CP when there were post-procedure complications.

We performed additional surgery after the endoscopic procedure in 11 cases when we failed to determine the depth of invasion during a procedure or confirmed to change pathology diagnosis after the procedure. We performed these surgeries an average of 1 month (range, 14–71 days) after we confirmed the pathology results, and there were no complications related to the surgeries. We did not need to extend hospital stay unnecessarily to confirm pathologic results after EMR or ESD procedures. There was no difference in the final outcome after additional surgery after confirming the pathologic result after discharge.

At the beginning of the study, we saw more tumor-positive margins, which could have been because we performed EMR more often than ESD. Chang et al reported that the possibility of residual neoplasia is low in lesions with tumor-positive lateral margins.[10,11] This might be caused by using coagulation during EMR or ESD which ablate remained residual neoplastic cells.[12] We confirmed residual neoplasia through careful follow-up endoscopy. All patients who underwent an endoscopic procedure within 2 days in the hospital underwent a first follow-up endoscopy at 4.9 months after the procedure, and we performed an average of 4.4 endoscopic examinations for 7.16 years. On periodic follow-up of the 168 patients with tumor-positive margins, 13 (7.4%) underwent additional ESD and 7 (4.0%) underwent surgery; there were no recurrences after the ESD procedures.

Although EMR and ESD techniques and instruments have improved, post-procedure complications and residual neoplasia are the major reasons for prolonged hospital stays and high medical costs.[13,14] Complications include bleeding, perforation, and aspiration pneumonia, with bleeding being the most common .[8,15]

Bleeding-related to endoscopic procedures is generally either intra- or post-procedure. Immediate bleeding and post-procedure delayed bleeding were reported as 2.9% and 3.9% of cases, respectively.[16] Although 50% to 70% of delayed bleeding is observed within 2 days of EMR or ESD, bleeding can develop as late as 2 weeks after the procedures.[17,18] At our hospital, 4 patients (0.4%) out of the 914 who had their procedures within 2 days at the hospital had post-procedure bleeding after discharge; the bleeding manifested as hematemesis or melena, but it was minor and could be controlled with endoscopic clipping or argon plasma coagulation. Three patients who had ESD received an average of 3 pack transfusions. There was no significant difference in the ratio of EMR or ESD among patients discharged from the 2 days' hospital stay. The bleeding was higher in the ESD group and the attention to bleeding during ESD treatment would be needed. Although the procedure method is important, the experience and skill of the operator will affect the safety of EMR or ESD.

To date, some risk factors have been recognized, such as the large resection sizes, long procedure time, location of lesion. The reason why larger lesions cause more bleeding is considered to be simply the fact that more blood vessels will be exposed after the large resection. Also, it took longer time when bleeding was frequent during the procedure or it was difficult to control the bleeding.[19] It has been generally reported that the lower part of the stomach is a risk factor for post-ESD bleeding.[20] The reasons for this remain unclear, but antral peristaltic activity and the alkaline effect of bile juice reflux may contribute to some extent.

In this study, the patient with bleeding after EMR had had a percutaneous coronary intervention 3 years earlier, and he took aspirin and clopidogrel. He stopped the aspirin 5 days before the EMR and began taking medication 3 days after the procedure, and he was admitted with hematochezia on the first day of resumption.

The possibility that antiplatelet agents are risk factors for procedure-related bleeding is controversial.[17,21,22] The 2014 guidelines of the Japan Gastroenterological Endoscopy Society and the American Society for Gastrointestinal Endoscopy recommend the continuous use of aspirin during endoscopic procedures in patients who are at high risk for thrombosis even if the procedures carry a high risk of bleeding.[23,24]

Second-look endoscopy is not recommended for delayed bleeding prevention because it is known to have no effect on clinical outcomes, including bleeding and morbidity after EMR and ESD.[25–27] One of the 3 patients who had bleeding had diabetes, and the other 2 had no special medical history.

Procedure related perforation or aspiration pneumonia was not observed in this study. Since we introduced CP, we stopped the protocol with a total of 440 patients who were then hospitalized for more than 2 days (post-procedure abdominal pain: n = 217 [49.3%], to confirm pathology results and for additional treatment: n = 85 [19.3%], post-procedure bleeding: n = 68 [15.5%], post-procedure perforation: n = 61 [13.9%], aspiration pneumonia: n = 8 [1.8%]). This study has some limitations. First, this was a retrospective study that assessed the outcomes of EMR or ESD within 2 days' hospital stay. Therefore, the retrospective nature of the review may have caused a potential bias in the analysis. Second, we did not directly compare the post-procedure outcome of patients who were discharged within 2 days and patients who were hospitalized for more than 2 days. Third, we did not analyze the type of procedure, number of procedures, complications and follow up results depending on the endoscopist. Fourth, although the safety of EMR or ESD according to size was not evaluated in this study, it is expected that the complications will increase as the size increases. Fifth, we did not evaluate the duration of drug discontinuation before the procedure of patients taking anticoagulants or antiplatelets.

For this study, we analyzed gastric neoplasia patients who underwent EMR or ESD within 2 days at our hospital over 10 years. If there is no special problem until the next day after the procedure, discharge without extension of the number of days of hospitalization will reduce the medical economic cost without any significant impact on the prognosis of the disease. The complications after the procedure were easily controlled, and the pathology results had little effect on the additional treatment plan; that is, performing the procedure within 2 days in hospital did not have significant effects on patients' prognoses. Since additional procedures or surgery required after tissue confirmation were also performed relatively quickly, there will be no need to extend the hospitalization for additional procedures or tissue confirmation.

In conclusion, EMR and ESD within 2 days in the hospital is effective and safe therapy for managing gastric neoplasia.

Author contributions

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