Original Article

Clinical outcome of non-curative endoscopic submucosal dissection for early gastric cancer

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Background: Early gastric cancer (EGC) is defined as cancer cells confined to the mucosal or submucosal layer, irrespective of size or presence of lymph node metastasis. The recent EGC endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR) guidelines (2021 Japan Gastroenterological Endoscopy Society (JGES) guidelines, 2nd edition) revised the concept from "endoscopic curative/non-curative resection" (NCR) to "endoscopic curability (eCura)". Under this, eCuraA and eCuraB signify curative resections (CRs), while eCuraC (including eCuraC-1 and eCura-C2) indicate NCRs. This study retrospectively analyzes clinical and pathological data from EGC patients who underwent endoscopic resection, assessing the long-term clinical outcomes in a substantial cohort after undergoing NCR.

Methods: We retrospectively analyzed clinical and pathological data from 443 EGC patients, encompassing 478 lesions, who received endoscopic treatment. The long-term clinical outcomes of patients who underwent NCR were statistically evaluated. Characteristics of the NCR group were compared with those of the surgical group, employing single- and multi-factor logistic regression analyses to identify risk factors that necessitate further surgical intervention. Prognostically, the Kaplan-Meier method and Log-Rank test determined the impact of risk factors on recurrence-free survival post-surgery in NCR patients. Differences were assessed using a method incorporating statistically significant differences in the multi-factor Cox regression analysis, evaluating the hazard ratio (HR) for disease recurrence following NCR.

Results: In this study, 443 EGC cases were pathologically diagnosed, comprising a total of 478 lesions. Of these, 127 cases underwent non-curative endoscopic resection, resulting in a NCR rate of 24.4%. Long-term follow-up was achieved for 117 (92.12%) patients. The metastasis/recurrence rate at 6 months stood at 23.1%. Multivariate Cox regression analysis identified lesion size ≥2.0 and <3 cm [P=0.02, HR =0.12, 95% confidence interval (CI): 0.02–0.67], presence of ulceration (P=0.03, HR =5.48, 95% CI: 1.23–24.33), lymphatic invasion (P=0.05, HR =17.51, 95% CI: 1.07–286.23), positive vertical margins (P=0.09, HR =3.77, 95% CI: 0.81–17.53), and flat macroscopic morphology (P=0.048, HR =4.8, 95% CI: 1.01–22.73) as independent risk factors for recurrence-free survival post non-curative endoscopic resection in EGC patients.

Conclusions: The recurrence/metastasis rate in patients who underwent NCR is notably higher compared to the control group. Significant prognostic risk factors include tumor size ≥2.0 and <3 cm, positive vertical margins, lymphatic invasion, and flat type (one of pathological gross classification). Patients in the eCuraC-2 category of NCR should consider further surgical intervention. The necessity for additional surgical

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intervention in these patients warrants further investigation.

Keywords: Early gastric cancer (EGC); non-curative resection (NCR); endoscopic resection; prognosis

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Introduction

Gastric cancer is the fourth most prevalent cancer globally and holds the second rank in cancer-related mortality worldwide (1-3). The clinical staging of gastric cancer is crucial in determining its outcome and prognosis. Early gastric cancer (EGC), when managed via endoscopic or surgical resection, can attain a 5-year survival rate exceeding 90%. Conversely, patients with advanced gastric cancer often experience a low rate of curative resection (CR), diminished quality of life, and a 5-year tumor-related survival rate below 30% (4).

In recent years, the paradigm for gastric cancer treatment has shifted. Traditionally, surgical resection was the mainstay of gastric cancer treatment. However, with the advent and widespread adoption of endoscopic resection techniques, these are now deemed the standard approach for treating EGC in patients with minimal risk of lymph node or distant metastasis. Endoscopic resection encompasses endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). Advances in endoscopic diagnostic and therapeutic technologies have markedly enhanced the early detection rates of EGC. Extensive multi-center studies indicate that endoscopic resection, compared to traditional surgery, offers benefits such as reduced trauma, fewer complications, and improved postoperative survival quality, making it the preferred treatment for EGC patients.

EGC assessment for curability after endoscopic resection is linked to local factors and the risk of lymph node metastasis. The 2021 Japanese Gastric Cancer Association (JGES)'s guidelines (5) for EGC ESD/EMR suggest comparable or improved long-term outcomes with endoscopic resection over surgical resection. These guidelines redefined the concept of "endoscopic curative/non-curative resection" (NCR) to "endoscopic curability (eCura)". Under this, eCura A and eCura B are categorized as CRs, while eCuraC, including eCuraC-1 and eCura-C2, are categorized as NCRs. eCura A includes: (I) predominantly differentiated type cancer, pT1a, UL0, unlimited tumor diameter, no lymphatic vessels and vascular invasion (Ly0, V0), *en bloc* resection, HM0, VM0; (II) mainly differentiated type, pT1a, UL1, tumor diameter ≤3 cm, Ly0, V0, *en bloc*, HM0, VM0. eCura B comprises of: (I) predominantly undifferentiated type, pT1a, UL0, tumor diameter ≤2 cm, Ly0, V0, *en bloc*, HM0, VM0; (II) mainly differentiated type, pT1b (SM1), ≤3 cm diameter, Ly0, V0, *en bloc*, HM0, VM0. eCuraC-1 includes differentiated type cancer meeting all criteria except *en bloc* resection or HM1. Treatments meeting eCura A/B but not eCuraC-1 criteria are classified as eCuraC-2 (5). For the definition of NCR, for example, there is a lack of clinical evidence for cases of differentiated type cancer combined with undifferentiated components. The goal of endoscopic resection for EGC is "CR", If NCR is achieved, additional treatment is necessary due to local recurrence and lymph node metastasis, typically involving surgical resection and lymph node dissection. However, in cases like refusal of surgery due to extended life

Highlight box

Key findings
- The study analyzes 10-year outcomes of non-curative resections (NCRs) for early gastric cancer (EGC) at Beijing Friendship Hospital, leveraging clinical and pathological data.

What is known and what is new?
- Additional surgical treatment following NCR of EGC including partial gastrectomy or lymph node dissection has shown lower recurrence/metastasis in previous studies.
- This study included 127 patients clinically and pathologically diagnosed with EGC who underwent non-curable resection after endoscopic submucosal dissection (ESD)/endoscopic mucosal resection (EMR) treatment and obtained specific results. Lymph node invasion as an important risk factor for poor prognosis requiring further surgery.

What is the implication, and what should change now?
- Current research underscores lymphatic involvement as critical in deciding additional surgery post-ESD/EMR in EGC, necessitating multi-faceted evaluation and acknowledging the future role of molecular diagnostics.

expectancy, comorbidities, poor overall health, or increased elderly patient proportion, NCR patients can opt to redo ESD, argon plasma coagulation (APC), or have regular follow-up without further treatment (6).

Although numerous studies have examined the long-term clinical outcomes of NCR patients undergoing ESD for EGC, research on a large population remains scarce. This retrospective study aims to investigate the risk factors influencing recurrence-free survival in NCR patients, with the objective of offering valuable insights for clinical assessment and preventive strategies. We present this article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-168/rc).

Methods

Inclusion/exclusion criteria

This study analyzed EGC cases treated with endoscopic therapy at the Digestive Endoscopy Center of Beijing Friendship Hospital, Capital Medical University from September 2012 to January 2020. We adhered to the criteria outlined in the latest Japanese Early Gastric Cancer ESD/EMR Guidelines (2021 JGES Guidelines, 2nd edition) (5). The inclusion criteria were: (I) positive horizontal/vertical margin; (II) submucosal infiltration depth ≥500 μm; (III) lymphatic/blood vessel invasion; (IV) undifferentiated type (undifferentiated cancer component, mucinous adenocarcinoma, or signet ring cell carcinoma); (V) non-*en-bloc* resection. The exclusion criteria included: (I) residual gastric cancer; (II) concurrent malignant tumors elsewhere; (III) incomplete clinical or endoscopic data; (IV) follow-up <6 months.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was reviewed and approved by Beijing Friendship Hospital, Capital Medical University (No. 2018-P2-058-01). The patients/participants provided their written informed consent to participate in this study.

Data collection

Patient demographics, endoscopic findings [lesion size, location, macroscopic appearance per Paris classification (7) and 2005 Paris Classification Standard Update (8)], procedural features (ESD approach: standard *vs.* hybrid ESD, *en bloc* resection), and pathologic outcomes {Vienna classification (9), depth of invasion [mucosa (M) and submucosa (SM), including SM1 (depth of submucosa infiltration of tumor tissue <500 μm), SM2 (depth of submucosa infiltration of tumor tissue ≥500 μm)] (7), margins [vertical margins (VM) and horizontal margins (HM)], lymphatic vessels invasion [lymph (Ly) and vascular (V)]} (7) from endoscopic specimens were gathered. For surgical patients, pathologic outcomes including residual neoplasia at the resection site, lymph node involvement, and post-surgical stage were recorded. Follow-up data, such as local recurrence, metastatic disease, and vital status at the last follow-up, were also collected. The end of follow up was marked by the last endoscopy and/or imaging study [computed tomography (CT) scan or others]. Recommended post-endoscopic treatment follow-up included gastroscopy at 3-, 6-, and 12-months post-surgery, then annually. For cases indicated as eCuraB resection, follow-up entailed esophagogastroduodenoscopy, along with ultrasound or abdominal-pelvic CT for metastatic tumors.

Definitions and outcomes

Under white light endoscopy, EGC typically presents with distinct features such as clear boundaries, irregular surface (10), changes in local mucosal color (red sign or fading), interrupted mucosal folds, and concentrated shallowness (11). An *en bloc* resection is defined as the removal of a lesion in one piece, and a complete resection (R0) is an *en bloc* resection with negative margins (deep or lateral) upon histological examination. Post-ESD, NCR patients were either part of the surgery group, undergoing operations with curative intent, or the follow-up group, based on multi-disciplinary treatment (MDT) recommendations and patient choice. Primary outcomes included disease recurrence, death, or disease-related death rates post non-curative ESD in both groups. Recurrence was categorized as: (I) local recurrence, identified as tumor lesions at the original resection site or within 1 cm of the surrounding area after more than 6 months post-surgery; (II) recurrence-free survival, defined as no residual tumor lesions within 6 months or absence of recurrence/metastasis post 6 months; (III) recurrence-free survival period, defined as the duration from ESD surgery to local/distant cancer recurrence, death, or last follow-up.

Statistical analysis

Data were managed and analyzed using SPSS 24.0

Table 1 Endoscopic baseline characteristics of included patients

Parameter	NCR patients (n=117), n (%)
Resection	
En bloc	97 (82.9)
Piecemeal	20 (17.1)
Depth of invasion	
Mucosa	73 (62.4)
SM1	25 (21.4)
SM2	19 (16.2)
Margin	
Clear margin	49 (41.9)
Positive lateral margin only	19 (16.2)
Positive vertical margin only	33 (28.2)
Positive lateral & vertical margin	16 (13.7)
Lymphatic invasion	45 (38.5)
Vascular invasion	29 (24.8)
eCura score	
Low risk	47 (40.1)
Medium risk	46 (39.3)
High risk	23 (19.6)
eCura	
eCuraC-1	43 (36.8)
eCuraC-2	74 (63.2)
Recurrence/metastasis	27 (23.1)
Post-surgery	42 (35.9)

NCR, non-curative resection; SM, submucosa; eCura, endoscopic curability.

software. Normally distributed continuous variables were represented as $\bar{x}\pm s$, and categorical variables as frequency and percentage. Chi-square test or Fisher's exact test were used for inter-group comparisons. Factors with statistical significance were further analyzed using multiple-factor logistic regression, presented as odds ratio (OR) values with their 95% confidence interval (CI). Kaplan-Meier method was used to plot survival curves, with differences compared using the log-rank test. Cox univariate regression identified factors affecting non-recurrent survival, and multiple-factor Cox analysis pinpointed independent risk factors, with P<0.05 indicating statistical significance.

Results

Baseline characteristics

Table 1 details the clinical and pathological features of NCR cases. Of the 127 NCRs, 10 were lost to follow-up, leaving 117 cases for the prognosis factor analysis. Among these, non-whole block piecemeal resections were observed in 20 cases (17.1%); SM2 tumor infiltration in 19 cases (16.2%), and SM1 in 25 cases (21.4%). Positive horizontal and vertical margins were found in 16 cases (13.7%), positive vertical margins only in 33 cases (28.2%), and positive horizontal margins only in 19 cases (16.2%). Recurrence/metastasis occurred in 27 cases (23.1%). Post-surgery, 42 out of 117 NCR patients with EGC (35.9%) underwent additional surgical procedures. eCura score distribution included 47 cases in the low-risk group (40.1%), 46 in the moderate-risk group (39.3%), and 23 in the high-risk group (19.6%).

Follow-up results of enrolled cases

The recurrence rate in the NCR group was significantly higher compared to the CR group, as indicated in *Table 2* (P<0.001). Kaplan-Meier analysis was used to construct survival curves, shown in *Figure 1*, with the red curve representing the CR group, and green curve representing the NCR group. We observed that recurrence rate of CR group was lower than NCR group, with P=0.002. Additionally, 42 of the 117 NCR patients (35.9%) underwent further surgical operations post-surgery. The study also compared the recurrence rates between the surgical and non-surgical groups, as shown in *Figure 2*, revealing a significant statistical difference (P=0.004).

EGC patients who underwent NCR with or without additional surgical procedures have clinical pathological characteristics

As shown in *Table 3*, in the NCR cohort, 42 patients, including 35 males and 7 females, underwent additional surgical procedures, which showed a statistical difference between genders (P=0.02). In terms of age, patients ≥60 years were more prevalent in the non-surgical than the surgical group (P=0.004). The surgical group had a higher proportion of undifferentiated pathology compared to the non-surgical group (P=0.008). Additionally, a greater proportion of patients in the surgical group had submucosal infiltration (P=0.02), and a higher prevalence of eCuraC-2 was observed in the surgical group (P<0.001). There were

Table 2 Baseline clinical and endoscopic profiles of patients categorized by management after ESD

Parameter	Total (n=117)	Surgery (n=42)	P value
Gender, male, n (%)	81(69.2)	35(83.3)	0.02
Age, ≥60 years, n (%)	89 (76.1)	25 (59.5)	0.004
Pathology, undifferentiated, n (%)	27 (23.1)	16 (38.1)	0.008
Ulcer, n (%)	46 (39.3)	18 (42.9)	0.70
Depth of invasion, SM, n (%)	43 (36.8)	22 (52.4)	0.02
Lymphatic invasion, n (%)	45 (38.5)	17 (40.5)	0.90
Vascular invasion, n (%)	29 (24.8)	12 (28.6)	0.63
Positive lateral margin, n (%)	35 (29.9)	11 (26.2)	0.09
Positive vertical margin, n (%)	49 (41.9)	23 (54.8)	0.06
Gross type, n (%)			0.007
Elevated	58 (49.6)	14 (33.3)	
Flat	19 (16.2)	6 (14.3)	
Depressed	40 (34.2)	22 (52.4)	
Tumor size (cm), n (%)			0.052
<2	51 (43.8)	13 (31.2)	
≥2 & <3	38 (32.6)	13 (31.2)	
≥3	27 (23.6)	16 (37.6)	
eCura, n (%)			<0.001
eCuraC-1	43 (36.8)	6 (14.3)	
eCuraC-2	74 (63.2)	36 (75.7)	
eCura score, n (%)			0.10
Low risk	48 (41.0)	12 (28.6)	
Medium risk	46 (39.3)	19 (45.2)	
High risk	23 (19.7)	11 (26.2)	

ESD, endoscopic submucosa dissection; SM, submucosa; eCura, endoscopic curability.

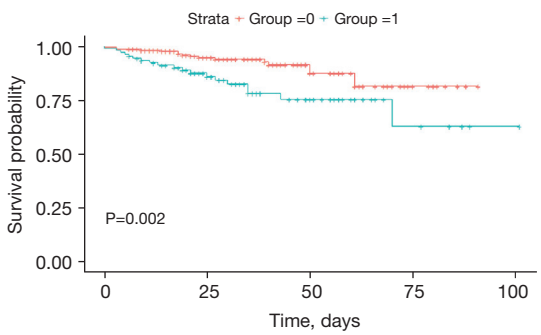

Figure 1 Recurrence survival curve for the curative resection group (Group 0) and non-curative resection group (Group 1).

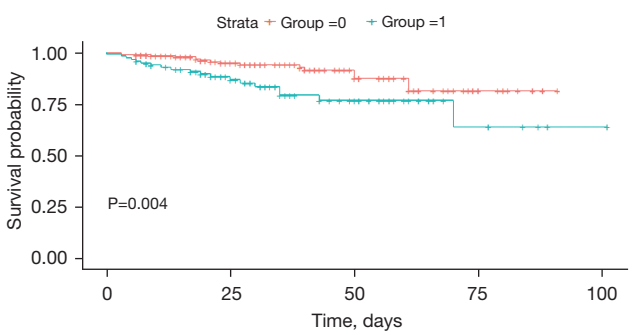

Figure 2 Recurrence survival curve for the surgical group (Group 1) and non-surgical group (Group 0).

Table 3 Basic and endoscopic factors in non-curative resection surgery group for early gastric cancer (n=42 cases)

Parameter	Muti-logistic regression		P value
	OR	95% CI	
Gender, male	0.314	0.096–1.029	0.06
Age, ≥60 years	0.230	0.074–0.712	0.01
Undifferentiated	2.263	0.764–6.706	0.14
Depth of invasion, SM	2.542	0.813–7.950	0.11
Positive lateral margin	1.539	0.459–5.156	0.49
Positive vertical margin	1.844	0.676–5.032	0.23
Gross type			0.02
Flat	1.282	0.313–5.257	0.73
Depressed	4.746	1.554–14.495	0.006
eCura			
eCuraC-1	0.059	0.009–0.374	0.003
eCuraC-2	0.172	0.032–0.929	0.04

SM, submucosa; OR, odds ratio; CI, confidence interval; eCura, endoscopic curability.

no statistical differences between surgical and non-surgical groups in terms of ulceration, lymphatic vessels/vascular infiltration, and positive horizontal and vertical margins.

Logistic multivariate regression analysis, including the aforementioned statistically significant factors, identified age <60 years (P=0.01), gross pathology type as concave (P=0.006), and eCuraC-2 (P=0.04) as independent risk factors for additional surgical procedures after NCR.

NCR prognostic factors (Cox univariate and multivariate regression)

Kaplan-Meier analysis was performed on the prognosis of patients with EGC who underwent NCR. Factors including surgical operation status, intra-operative persistent bleeding, family history of tumors, resection method, lymphatic and vascular invasion, pathological differentiation, and endoscopic observation of white moss, as well as horizontal/vertical margin status, showed statistical differences in the prognosis following NCR. These factors were then included in univariate Cox regression analysis as detailed in *Table 4*. The analysis revealed that the family history of tumors, lesion size, presence of ulcers, white moss observed during endoscopy, persistent bleeding during surgery, treatment method, lymphatic invasion, positive vertical margin, and pathological gross type (flat type) significantly impacted the 6-month disease-free survival of patients with EGC who underwent NCR via endoscopy. Furthermore, multivariate Cox regression analysis identified lesion size postoperative ≥2 & <3 cm, presence of ulcers, lymphatic invasion, positive vertical margin, and pathological gross type (flat type) as independent risk factors affecting the disease-free survival of these patients. Detailed findings are available in *Table 4*.

Discussion

The advancement and widespread adoption of early screening and minimally invasive endoscopic techniques have led to the increased detection and treatment effectiveness of EGCs (12). Previous large-scale clinical study has demonstrated that endoscopic resection offers higher long-term survival rates and lower recurrence rates compared to traditional surgical methods, thus enhancing patients' quality of life (13). If the patients with early gastric cancer treated by endoscopy cannot meet the standard of CR after the standard pathological evaluation of the resected lesion, it is considered as NCR (14,15). This study focuses on the long-term follow-up and analysis of clinical outcomes for patients with NCR of EGC.

This study analyzed the recurrence rate and its risk factors in NCRs. The local recurrence rate post NCR was 23.1%, with a median follow-up of approximately 24 months, which was significantly higher than the CR

Table 4 Univariate and multivariate Cox regression analysis of non-curable resection recurrence

Parameter	Univariate Cox regression		Multivariate Cox regression	
	HR (95% CI)	P	HR (95% CI)	P
Gender, female	1.05 (0.45–2.43)	0.92		
Age, ≥60 years	1.83 (0.63–5.29)	0.27		
Lesion size (cm)				
<2	1			
≥2 & <3	0.24 (0.07–0.84)	0.03	0.12 (0.02–0.67)	0.02
≥3	0.49 (0.14–1.69)	0.26	2.07 (0.4–10.84)	0.39
Tumor histopathology				
Differentiated	1			
Undifferentiated	1.71 (0.74–3.91)	0.21		
Ulcer	6.88 (2.59–18.28)	<0.001	5.48 (1.23–24.33)	0.03
Remarkable redness	1.92 (0.88–4.2)	0.10		
Gross morphology	1.74 (0.41–7.42)	0.45		
Margin elevation	0.46 (0.16–1.36)	0.16		
Enlarged folds	0.60 (0.08–4.45)	0.62		
Uneven surface	0.43 (0.2–0.96)	0.04	0.3 (0.06–1.59)	0.16
Nodularity	0.27 (0.04–1.98)	0.20		
White moss	2.68 (1.05–6.87)	0.04	6.16 (0.58–65.74)	0.13
Bleeding	5.49 (1.24–24.35)	0.03	0.41 (0.02–8.91)	0.57
Resection				
En bloc	1			
Piecemeal	0.88 (0.3–2.55)	0.81		
Treatment				
ESD	1			
EMR	6.14 (0.83–45.72)	0.08		
Lymphatic invasion	6.67 (2.66–16.73)	<0.001	17.51 (1.07–286.23)	0.045
Vascular invasion	1.62 (0.72–3.65)	0.24		
Positive horizontal margin	1.45 (0.76–2.78)	0.26		
Positive vertical margin	14.6 (4.41–48.93)	<0.001	3.77 (0.81–17.53)	0.09
Depth of invasion (μm)				
<500	1			
≥500	0.81 (0.28–2.36)	0.70		
Gross type				
Elevated	1			
Flat	3.16 (1.26–7.92)	0.01	4.8 (1.01–22.73)	0.05
Depressed	1.29 (0.52–3.23)	0.60	0.62 (0.15–2.59)	0.51
eCura score				
Low risk	1			
Medium risk	1.45 (0.57–3.73)	0.44	0.24 (0.02–2.63)	0.24
High risk	2.78 (1.05–7.36)	0.04	0.23 (0.02–2.97)	0.26

HR, hazard ratio; CI, confidence interval; ESD, endoscopic submucosal dissection; EMR, endoscopic mucosal resection; eCura, endoscopic curability.

group's 5.3% recurrence rate. Factors influencing local recurrence included submucosal infiltration, positive vertical margins, and lymphatic vessel invasion, aligning with previous research findings. A study of 152 non-curatively resected EGC cases indicated a higher risk of local recurrence after piecemeal endoscopic resection, especially in cases exceeding ESD criteria with lymphatic vessel invasion (16). Although many studies consider lymph node invasion as an important risk factor for poor prognosis requiring further surgery, a recent study that surveyed 15 lesions regarding lymph node metastasis rate for lymphovascular infiltration, which only detected one lesion (6.7%), showed that lymphovascular invasion does not necessarily indicate lymph node metastasis (17). Patients diverging from CR norms solely on lymphovascular invasion may have lesions unnecessary for further surgery. Additional confirmation is needed in treating deviations based solely on lymphovascular criteria. In our research, postoperative lesion size ≥3 cm, ulceration, lymphatic vessel invasion, and positive vertical margins emerged as independent risk factors impacting recurrence-free survival in NCR patients (18). Previous researches indicated that submucosal invasion, lymphovascular presence, and undifferentiated histology are valid surgical management indicators (19-23). Hence, we compared the survival of surgical and non-surgical groups. The survival curve indicated a significant statistical difference in the recurrence rate between these two groups (P=0.004). In the long-term follow-up of 71 cases diagnosed with EGC by endoscopy, who did not undergo surgical resection or were diagnosed more than 6 months post-surgery, the cumulative risk of progression to advanced cancer after 5 years was 63.0% (95% CI, 48–78%). Additionally, a statistical analysis was conducted between the surgical and non-surgical groups. Univariate analysis revealed significant gender differences, with a higher prevalence of males (P=0.02). More individuals aged ≥60 years were found in the non-surgical group compared to the surgical group (P=0.004). Pathologically, the surgical group had a higher incidence of undifferentiated cases than the non-surgical group (P=0.008). Regarding invasion depth, the surgical group had more submucosal layer cases than the non-surgical group (P=0.02), and a higher proportion of eCuraC-2 (P<0.001). No statistical differences were observed between the groups in terms of ulceration, lymphatic vessel invasion, and positive horizontal and vertical margins. Aligning with latest guidelines, multivariate regression analysis identified age ≥60 years (P=0.01), depressed gross type (P=0.006), and eCuraC-2 (P=0.04) as independent risk factors for NCR necessitating further surgery. In addition to these factors evaluated in this study, a recent study by Japanese scholars pointed out that additional gastrectomy after non-curative ESD for pT1 EGC could provide an oncologically safe outcome (24). With the continuous development of endoscopic technology, an increasing number of expanded ESD are being performed. Although this study only compared patient information for selecting surgical procedures, a recent meta-analysis of all available and most updated studies comparing ESD versus surgery for the treatment of uEGC found that all-cause mortality was similar in both groups after adjusted analyses (25). A recent South Korean study delved into the risks and advantages of extra surgery for upper third EGC post non-curative ESD, identifying lymphovascular invasion as the sole significant predictor of lymph node metastasis (P<0.001) (26). And a Japanese study that included 151 patients diagnosed with noncurative lesions after ESD treatment over the past decade recommended gastrectomy and lymph node dissection for patients with lymphatic vessel invasion and/or undifferentiated types (27). But Katsuragi *et al.* point out that clinicians advise additional gastrectomy if pathological analysis of ESD specimens shows lymphovascular infiltration by tumors. However, subsequent gastrectomy based on this pathological assessment often fails to reveal any lymph node metastasis (28). In our previous study, we have showed the size of NCR lesions were 2.32±1.30 cm (29), and the pathological evaluation was carried out in accordance with the guidelines, the specimen was cut in parallel at an interval of 2–3 mm perpendicular to the nearest incisal edge of the specimen. In this cohort, there are 5/42 (11.90%) cases with lymph node involvements revealed by surgical resection after non-curative ESD. Consistent with previous studies (13,26), our results show that the additional surgery group has a better prognosis in the long run. In clinical practice, the choice of treatment strategy is influenced by efficacy and risk of recurrence/metastasis, age, baseline physical condition, postoperative quality of life, patient or family preferences, and financial status. Additionally, several articles have indicated that high-risk comorbidities are given greater consideration from the patient's perspective in treatment decisions (30,31). A retrospective study demonstrated that high-risk comorbidity [Charlson Comorbidity Index (CCI) ≥3] was an independent prognostic factor (30). In conclusion, for EGC patients at high risk for recurrence/metastasis after non-curative ESD, additional surgical treatment should be determined through multi-faceted evaluation by the attending pathologist,

endoscopist, surgeon and patients and molecular diagnosis should not be ignored.

This study has several limitations: (I) being a single-center study with a relatively small sample size, it may not fully represent the broader population. Additionally, some endoscopy and pathology reports from the early years [2012–2014] lack the standardized content mentioned in this article. The results could be influenced by the limited case number and the uneven distribution of pathological types, necessitating further validation through multi-center studies with larger sample sizes. (II) As a retrospective study spanning ten years that is based on gastric endoscopy cases from the Digestive Endoscopy Center of Beijing Friendship Hospital, Capital Medical University, there are inherent limitations. Despite careful data selection, achieving consistency among surgical operators and endoscopy report standards is challenging. Furthermore, not all pathological results were evaluated by the same pathologist, which may introduce bias and affect the study outcomes. (III) Some data incompleteness may lead to bias in statistical analysis.

Conclusions

In conclusion, the recurrence/metastasis rate in the NCR group is significantly higher than that in the control group. Prognostic risk factors include tumor size ≥2 & <3 cm, positive vertical margins, lymphatic invasion, and flat type (one of pathological gross classification). Patients with NCR and eCuraC-2 should consider additional surgical intervention.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-168/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was reviewed and approved by Beijing Friendship Hospital, Capital Medical University (No. 2018-P2-058-01). The patients/participants provided their written informed consent to participate in this study.

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