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Retrospective Study

Factors associated with overall survival in early gastric cancer patients who underwent additional surgery after endoscopic submucosal dissection

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Abstract

BACKGROUND

Controversy exists about the benefit of additional surgery after endoscopic submucosal dissection (ESD) for early gastric cancer (EGC).

AIM

To examine risk factors for overall survival (OS) after additional surgery in patients with EGC who initially underwent ESD.

METHODS

This was a retrospective analysis of patients with EGC who underwent additional surgery after ESD at the Beijing Friendship Hospital affiliated to Capital Medical University between August 2012 and August 2019. OS was the primary outcome. Lymph node metastasis and residual tumor were secondary outcomes. Logistic regression models and Kaplan-Meier curves were used for further analysis.

RESULTS

Forty-two patients were evaluated, including 35 (83.3%) males and 7 (16.7%) females. The mean age was 62 (range, 32-82) years. Male sex [hazard ratio (HR) = 21.906, 95% confidence interval (CI): 3.762-229.250; $P = 0.039$], T1b invasion (HR = 3.965, 95% CI: 1.109-17.432; $P = 0.047$), undifferentiated tumor (HR = 9.455, 95% CI: 0.946-29.482; $P = 0.049$), lymph node metastasis (HR = 2.126, 95% CI: 0.002-13.266; $P = 0.031$), and residual tumor (HR = 4.275, 95% CI: 1.049-27.420; $P = 0.043$) were independently associated with OS. The follow-up duration was 4-81 mo (median:

approved by the Ethics Committee of Beijing Friendship Hospital, Capital Medical University (Approval No. 2018-P2-015-02).

Informed consent statement:

Patients were not required to provide informed consent to the study because this was a retrospective study and only analyzed the clinical data of the patients. All patient data were analyzed after anonymization.

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50.7 mo). OS was 77.0 ± 12.1 mo (95%CI: 53.3-100.7 mo). The 3-year and 5-year OS rates were 94.1% and 85%, respectively.

CONCLUSION

Male sex, T1b invasion, undifferentiated tumor, lymph node metastasis, and residual tumor are independently associated with OS in patients with EGC who underwent additional surgery after ESD.

Key Words: Stomach neoplasms; Endoscopic submucosal dissection; Gastrectomy; Lymphatic metastasis; Neoplasm residual; Survival analysis

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Core Tip: This was a retrospective study examining risk factors for overall survival after additional surgery in patients with early gastric cancer who initially underwent endoscopic submucosal dissection, especially the effects of lymph node metastasis and residual tumor. The results indicated that male sex, T1b invasion, undifferentiated tumor, lymph node metastasis, and residual tumor were independently associated with overall survival in patients with early gastric cancer who underwent additional surgery after endoscopic submucosal dissection.

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INTRODUCTION

The incidence of gastric cancer (GC) is highest in Eastern Asia, Eastern Europe, and South America^[1,2]. GC affects men more than women^[1]. The direct cause of GC is unclear, but *Helicobacter pylori* infection and some hereditary cancer predisposition syndromes may play a role^[1]. Patients often present with nonspecific symptoms, which may include anorexia, weight loss, abdominal pain, dyspepsia, vomiting, and early satiety^[1,2]. With the improvement of public health awareness and the development of endoscopic and imaging technologies, the detection rate of early GC (EGC) among the overall GCs is increasing^[3,4]. Statistics from the China Gastrointestinal Cancer Surgery Union show that EGC accounts for 19.5% of all GCs in China^[5]. Therefore, the management of EGC warrants further study.

Current treatments for EGC include endoscopic mucosal resection/endoscopic submucosal dissection (EMR/ESD) and standard radical gastrectomy^[6,7]. Standard radical gastrectomy can achieve a good radical effect; however, due to the low lymph node metastasis rate of EGC, most patients undergo unnecessary or excessive lymph node dissection, which increases the surgical trauma^[6,7]. On the other hand, although EMR/ESD can completely remove the lesion, it cannot evaluate for possible metastasis in the gastric peripheral lymph node, which may lead to treatment failure^[6,7]. With the refinement of ESD indications, an increasing number of patients with EGC who meet the expanded indications undergo ESD^[8-11].

Nevertheless, whether patients not meeting the criteria for curative resection after ESD need further surgery remains largely controversial^[12-15]. A large-scale non-inferiority study^[16] found that endoscopic treatment can achieve the same results as surgery in the long run, but other studies have suggested that additional surgery is recommended in patients who underwent endoscopic non-curative resection^[17,18].

Therefore, factors associated with prognosis upon further surgery following ESD should be urgently explored, which would provide predictive value for clinical decisions. In this setting, the present study aimed to mainly examine risk factors for overall survival (OS) upon additional surgery in patients with EGC who initially underwent ESD, especially the impacts of lymph node metastasis and residual tumor. The results could provide a reference for clinicians to better select treatments for EGC

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patients.

MATERIALS AND METHODS

Study design and patients

This was a retrospective analysis of patients with EGC who underwent additional surgery after ESD at the General Surgery Center of Beijing Friendship Hospital affiliated to Capital Medical University between August 2012 and August 2019. This study was approved by the Ethics Committee of Beijing Friendship Hospital, Capital Medical University (No. 2018-P2-015-02). Because this was a retrospective study only analyzing clinical data, informed consent was waived. All patient data were analyzed after anonymization.

The inclusion criteria were: (1) Diagnosis of EGC^[7,19,20]; (2) Underwent additional radical surgery after ESD; and (3) Complete clinical data. The exclusion criteria were: (1) Gastric stump cancer, recurrent GC, multiple primary malignant tumors of the abdominopelvic cavity, or a history of other malignant tumors within 5 years; (2) Postoperative pathologically confirmed advanced GC ($pT_2N_{0-3}M_{0-1}$); or (3) Uncontrollable internal medicine diseases, including unstable angina pectoris, myocardial infarction, or cerebrovascular accident, within 6 mo.

ESD

All ESD procedures were performed by experienced endoscopic surgeons, who had completed at least 100 ESD surgeries independently. The surgical equipment included an Olympus GIF-Q260J single-channel therapeutic endoscope, a dual knife, an IT-knife, a hook knife, and a flex knife. ESD resection mainly comprised of three steps. First, a dual knife or an IT-knife was used to generate a circular mark along the edge of the lesion at least 5 mm away. Fluid was injected into the submucosa to fully separate the tumor lesion from the muscularis propria. Second, a dual knife or an IT-knife was used to circularly cut the mucosa around the lesion. Finally, the tumor lesion and submucosal connective tissue were completely dissected from the circular incision, and hemostasis of the wound was performed. The detailed surgical procedures have been thoroughly described in previous research reports^[21,22]. The collected specimens were fixed and examined by experienced pathologists.

Criteria for curative resection of ESD

The criteria for curative resection of ESD were: (1) Undifferentiated intramucosal carcinoma with no ulcer and a tumor size ≤ 2 cm; (2) Differentiated submucosal carcinoma T1b-SM1 with a tumor size ≤ 3 cm (submucosal invasion depth < 500 μ m); (3) Ulcerative, differentiated intramucosal carcinoma with a tumor size < 3 cm, accompanied by undifferentiated components; (4) Differentiated intramucosal carcinoma with no ulcer and a tumor size > 2 cm; and (5) Differentiated intramucosal carcinoma with no ulcer and a tumor size < 2 cm^[7,19]. After complete resection of the lesions, the horizontal and vertical resection margins were negative, with no blood vessels or lymphatic invasion. Otherwise, ESD was considered non-curative.

Additional radical surgery

In patients with EGC whose pathology did not meet the criteria for curative resection after ESD, radical surgery for GC was additionally performed. The interval between the two surgeries depended on the patient's physical conditions. Radical distal, proximal, or total gastrectomy was selected based on tumor location. All patients underwent standard D1 or D2 lymph node dissection, according to the specific conditions of the tumor. The specific procedures and range of lymph node dissection were based on the Japanese Gastric Cancer Treatment Guidelines 2018 (5th edition)^[7].

Outcomes

OS was the primary outcome of this study. OS was defined as the length of time from additional surgery to death from any cause. In patients undergoing non-curative resection, the treatment focused on two aspects: (1) Risk of lymph node metastasis; and (2) Risk of residual tumor (positive resection margin or local recurrence). Therefore, the above two aspects were considered secondary outcomes.

Data collection

Clinical data were extracted from medical charts, including sex, age, number of tumor

lesions, tumor location, general type, tumor size, histological type, Lauren classification, depth of invasion, pattern of invasion, horizontal resection margin, vertical resection margin, nerve invasion, vascular invasion, eCura score^[23], degree of radical endoscopic treatment (eCura), ulcer, surgical methods, range of lymph node dissection, and cancerous nodules.

The patients were assigned to two age groups (< 60 years *vs* ≥ 60 years) according to the age bracket proposed by the World Health Organization. The general type included the protruded, flat, and pitting types according to the Japanese Gastric Cancer Treatment Guidelines 2018 (5th edition)^[7]. Tumor size was determined as the largest tumor diameter. Histological types were divided into differentiated (including highly and moderately differentiated adenocarcinoma, tubular adenocarcinoma, and papillary adenocarcinoma) and undifferentiated (poorly differentiated adenocarcinoma, signet-ring cell carcinoma, and mucinous adenocarcinoma) types. Based on the depth of invasion, the tumors were divided into intramucosal carcinoma (T1a) and submucosal carcinoma (T1b). Among them, submucosal carcinoma was further classified into three subtypes according to the depth of tumor invasion: T1b-SM1 (submucosal invasion depth < 500 μm), T1b-SM2 (depth of 500-1000 μm), and T1b-SM3 (depth of 1000-1500 μm). The invasion patterns included INFa (tumor lesion grew expansively, showing a clear boundary with the surrounding tissues), INFb (growing status of tumor lesion between INFa and INFc), and INFc (tumor lesion grew invasively, showing an unclear boundary with the surrounding tissues). The eCura score included tumor size (1 point), invasion depth (1 point), lymphatic invasion (3 points), venous invasion (1 point), and positive vertical margin (1 point)^[23]. Based on eCura scores, the patients were divided into three groups: Low-risk (0-1 points), moderate-risk (2-4 points), and high-risk (5-7 points) groups. Based on the degree of radical endoscopic treatment (eCura), cases were assigned to the eCura-A (tumor completely resected, meeting the absolute indication for ESD), eCura-B (tumor completely resected for one time, meeting the relatively expanded indication for ESD resection), eCura-C1 (in differentiated carcinoma, other conditions of eCura A or B were met, but complete tumor resection or positive horizontal margin was not achieved), and eCura-C2 (none of the above conditions were met) groups.

Follow-up

The patients were followed every 6 mo after surgery. After discharge, follow-up was performed *via* outpatient visits, inpatient reexaminations, telephone calls, or mails. During the follow-up period, physical examination, laboratory tests (including routine blood tests, biochemical examinations, and gastrointestinal tumor markers), chest computed tomography (CT), abdominal and pelvic CT scans, and gastroscopy were performed annually. The follow-up period ended on December 31, 2019.

Statistical methods

SPSS 21.0 (IBM Corp., Armonk, NY, United States) was used for all statistical analyses. Categorical data are presented as frequencies and percentages, and were compared by the chi-square test, the corrected chi-square test, or the Fisher's exact test. Ranked data are expressed by frequencies and percentages, and were compared by the rank-sum test. Continuous data were tested for normal distribution using the Kolmogorov-Smirnov test. Those with a normal distribution are presented as the mean ± SD, and were analyzed using the Student *t*-test; those with a skewed distribution are presented as medians (interquartile ranges) and were analyzed using the Mann-Whitney *U*-test. Univariable and multivariable analyses were performed by Cox regression to determine the independent risk factors for OS. The stepwise method was used for multivariable Cox regression analysis. Survival analysis was performed using the Kaplan-Meier method and the log-rank test. *P* < 0.05 was considered statistically significant.

RESULTS

Characteristics of the patients

A total of 51 patients with EGC were eligible for this study. Nine patients were excluded: One with gastric stump cancer, one with ascending colon cancer 2 years ago, six with postoperatively pathologically confirmed advanced GC, and one elderly male patient with a history of acute cerebral infarction 5 mo before enrollment. Finally, 42 patients with EGC were eventually included in the study (Table 1). Among them, there were 35 (83.3%) males and 7 (16.7%) females, indicating a male to female ratio of 5:1.

Table 1 Characteristics of the patients

Clinicopathological factor	Total (n = 42)	Lymph node metastasis		Residual tumor			
		No (n = 37)	Yes (n = 5)	P value	No (n = 29)	Yes (n = 13)	P value
Age (yr), n (%)				0.926			0.513
< 60	16 (38.1)	14 (37.8)	2 (40.0)		12 (41.4)	4 (30.8)	
≥ 60	26 (61.9)	23 (62.2)	3 (60.0)		17 (58.6)	9 (69.2)	
Sex (male), n (%)	35 (83.3)	34 (91.9)	1 (20.0)	< 0.001	26 (89.7)	9 (69.2)	0.101
Tumor location, n (%)				0.316			0.360
Upper stomach	12 (28.6)	12 (32.4)	0 (0)		9 (31.0)	3 (23.1)	
Middle stomach	17 (40.5)	14 (37.9)	3 (60.0)		13 (44.8)	4 (30.8)	
Lower stomach	13 (30.9)	11 (29.7)	2 (40.0)		7 (24.2)	6 (46.1)	
Tumor size (cm), n (%)				0.281			0.862
< 2	9 (21.4)	7 (18.9)	2 (40.0)		6 (20.7)	3 (23.1)	
≥ 2	33 (78.6)	30 (81.1)	3 (60.0)		23 (79.3)	10 (76.9)	
Gross type, n (%)				0.207			0.106
Protruded	8 (19)	8 (21.6)	0 (0)		6 (20.7)	2 (15.4)	
Flat	7 (16.7)	7 (18.9)	0 (0)		7 (24.1)	0 (0)	
Pitting	27 (64.3)	22 (59.5)	5 (100.0)		16 (55.2)	11 (84.6)	
Surgical method, n (%)				0.322			0.152
Distal subtotal gastrectomy	26 (61.9)	21 (56.8)	5 (100.0)		15 (51.7)	11 (84.6)	
Proximal subtotal gastrectomy	8 (19)	8 (21.6)	0 (0)		6 (20.7)	2 (15.4)	
Total gastrectomy	3 (7.2)	3 (8.1)	0 (0)		3 (10.3)	0 (0)	
Celiac lymph node dissection	5 (11.9)	5 (13.5)	0 (0)		5 (17.3)	0 (0)	
Invasion depth, n (%)				0.018			0.307
T1a	19 (45.2)	19 (51.4)	0 (0)		13 (44.8)	6 (46.2)	
T1b	23 (54.8)	18 (48.6)	5 (100)		16 (55.2)	7 (53.8)	
Histological type, n (%)				0.028			0.654
Differentiated	27 (64.3)	26 (70.3)	1 (20)		18 (62.1)	9 (69.2)	
Undifferentiated	15 (35.7)	11 (29.7)	4 (80)		11 (37.9)	4 (30.8)	
Number of tumor lesions, n (%)				0.710			0.498
Solitary	41 (97.6)	36 (97.3)	5 (100.0)		28 (96.6)	13 (100.0)	
Multiple	1 (2.4)	1 (2.7)	0 (0)		1 (3.4)	0 (0)	
Positive vascular invasion, n (%)	5 (11.9)	0 (0)	5 (100.0)	< 0.001	0 (0)	5 (38.5)	< 0.001
Lauren classification, n (%)				0.039			0.532
Intestinal type	22 (52.4)	21 (56.8)	1 (20.0)		15 (51.7)	7 (53.8)	
Diffuse	13 (31.0)	9 (24.3)	4 (80.0)		8 (27.6)	5 (38.5)	
Mixed	7 (16.6)	7 (18.9)	0 (0)		6 (20.7)	1 (7.7)	
Pattern of invasion, n (%)				< 0.001			0.001
IFN-A	8 (19.0)	8 (21.6)	0 (0)		6 (20.7)	2 (15.4)	
IFN-B	26 (62.0)	26 (70.3)	0 (0)		22 (75.9)	4 (30.8)	
IFN-C	8 (19.0)	3 (8.1)	5 (100.0)		1 (3.4)	7 (53.8)	
Positive horizontal resection margin, n (%)	19 (45.2)	18 (48.6)	1 (20.0)	0.227	10 (34.5)	9 (69.2)	0.036
Positive vertical resection margin, n (%)	21 (50.0)	16 (43.2)	5 (100.0)	0.017	14 (48.3)	7 (53.8)	0.739

Positive nerve invasion, <i>n</i> (%)	4 (9.5)	1 (2.7)	3 (60.0)	< 0.001	0 (0)	4 (30.8)	0.002
eCura score, <i>n</i> (%)				< 0.001			0.007
Low-risk group	24 (57.1)	24 (64.9)	0 (0)		18 (62.1)	6 (46.2)	
Moderate-risk group	14 (33.3)	13 (35.1)	1 (20.0)		11 (37.9)	3 (23.1)	
High-risk group	4 (9.6)	0 (0)	4 (80.0)		0 (0)	4 (30.7)	
Degree of radical endoscopic treatment (eCura), <i>n</i> (%)				0.467			0.790
eCura-A	1 (2.4)	1 (2.7)	0 (0)		1 (3.5)	0 (0)	
eCura-B	1 (2.4)	1 (2.7)	0 (0)		1 (3.5)	0 (0)	
eCura-C1	11 (26.2)	11 (29.7)	0 (0)		7 (24.1)	4 (30.8)	
eCura-C2	29 (69.0)	24 (64.9)	5 (100.0)		20 (68.9)	9 (69.2)	
Ulcer, <i>n</i> (%)	26 (61.9)	22 (59.5)	4 (80.0)	0.375	16 (55.2)	10 (76.9)	0.180
Range of lymph node dissection, <i>n</i> (%)				0.409			0.101
D1	24 (57.1)	22 (59.5)	2 (40.0)		19 (65.5)	5 (38.5)	
D2	18 (42.9)	15 (40.5)	3 (60.0)		10 (34.5)	8 (61.5)	

The mean age was 62 (range, 32-82) years. The degree of radical endoscopic treatment was evaluated after ESD in all patients, including one with eCura A, one with eCura B, 11 with eCura C1, and 29 with eCura C2. All patients underwent standard radical gastrectomy or celiac lymph node dissection. Postoperative pathology revealed that there were 19 (45.2%) patients with tumor invasion to T1a, 6 (14.3%) to T1b-SM1, 15 (35.7%) to T1b-SM2, and 2 (4.8%) to T1b-SM3. There were 19 (45.2%) patients with highly differentiated adenocarcinoma, 8 (19.1%) with moderately differentiated adenocarcinoma, and 15 (35.7%) with poorly differentiated adenocarcinoma; 27 (64.3%) and 15 (35.7%) had differentiated and undifferentiated tumors, respectively. Five (11.9%) cases had vascular invasion and 37 (88.1%) had no vascular invasion. There were 4 (9.5%) patients with nerve invasion and 38 (90.5%) without nerve invasion.

Survival analysis

Among the 42 patients with EGC, the follow-up period was 4-81 mo, with a median duration of 50.7 mo. During follow-up, three (7.1%) patients were lost to follow-up. A total of five deaths occurred among all patients. One individual died of advanced age complicated with organ failure, with no tumor recurrence at death; the remaining four died of tumor recurrence or liver metastasis. OS was 77.0 ± 12.1 mo (95% confidence interval (CI): 53.3-100.7 mo). The 3-year and 5-year OS rates were 94.1% and 85%, respectively (Figure 1A).

Factors associated with OS

The three patients that were lost to follow-up were not included in survival analysis; therefore, 39 patients were assessed for risk factors for OS. As shown by the multivariable analysis, male sex [hazard ratio (HR) = 21.906, 95%CI: 3.762-229.250; $P = 0.039$], T1b invasion (HR = 3.965, 95%CI: 1.109-17.432; $P = 0.047$), undifferentiated tumor (HR = 9.455, 95%CI: 0.946-29.482; $P = 0.049$), lymph node metastasis (HR = 2.126, 95%CI: 0.002-13.266; $P = 0.031$), and residual tumor (HR = 4.275, 95%CI: 1.049-27.420; $P = 0.043$) were independently associated with OS (Table 2).

Survival analysis according to lymph node metastasis

The OS of patients with lymph node metastasis was 69.0 ± 2.7 mo (95%CI: 63.7-74.3), which was statistically different from that of patients without lymph node metastasis ($P < 0.001$) (Figure 1B). A total of 34 patients were followed for 3 years. The 3-year OS rate of those with lymph node metastasis was 60%, while individuals without lymph node metastasis all survived (OS rate of 100%). A total of 20 patients were followed for 5 years. The 5-year OS rate of patients without lymph node metastasis was significantly higher than that of patients with lymph node metastasis (100% vs 25%).

Survival according to residual tumor

The OS of patients with residual tumor did not reach the median survival time, but

Table 2 Independent risk factors for overall survival

Characteristic	Univariable analysis			Multivariable analysis		
	HR	95%CI	P value	HR	95%CI	P value
Age (yr)						
< 60	Reference	-	-	Reference	-	-
≥ 60	1.152	0.119-11.174	0.902			
Sex (male)	13.550	1.407-130.515	0.024	21.906	3.762-229.250	0.039
Tumor location						
Upper stomach	Reference	-	-	Reference	-	-
Middle stomach	2.740	0.563-13.340	0.212			
Lower stomach	2.124	0.417-13.101	0.197			
Tumor size (cm)						
< 2	Reference	-	-	Reference	-	-
≥ 2	0.222	0.031-18.579	0.133			
Gross type						
Protruded	Reference	-	-	Reference	-	-
Flat	0.000	0.000	0.984			
Pitting	1.440	0.149-27.959	0.753			
Invasion depth						
T1a	Reference	-	-	Reference	-	-
T1b	2.011	0.621-6.213	0.018	3.965	1.109-17.432	0.047
Histological type						
Differentiated	Reference	-	-	Reference	-	-
Undifferentiated	13.155	0.991-25.014	0.028	9.455	0.946-29.482	0.049
Number of tumor lesions						
Solitary	Reference	-	-	Reference	-	-
Multiple	0.912	0.301-9.761	0.781			
Positive vascular invasion	0.818	0.169-8.965	0.803			
Lauren classification						
Intestinal type	Reference	-	-	Reference	-	-
Diffuse	1.683	0.518-15.468	0.386			
Mixed	0.968	0.512-14.129	0.571			
Pattern of invasion						
IFN-A	Reference	-	-	Reference	-	-
IFN-B	0.545	0.080-33.730	0.537			
IFN-C	9.899	1.159-19.526	0.036			
Positive horizontal resection margin	0.989	0.164-45.987	0.990			
Positive vertical resection margin	29.109	0.172-353.649	0.353			
Positive nerve invasion	1.000	0.10-102.816	> 0.999			
eCura score						
Low-risk group	Reference	-	-	Reference	-	-
Moderate-risk group	0.938	0.126-27.910	0.810			
High-risk group	0.994	0.108-10.192	0.715			

Degree of radical endoscopic treatment (eCura)						
eCura-A	Reference	-	-	Reference	-	-
eCura-B	0.997	0.000	> 0.999			
eCura-C1	0.812	0.101-15.171	0.969			
eCura-C2	1.745	0.257-11.846	0.569			
Ulcer	0.829	0.134-13.122	0.840			
Range of lymph node dissection						
D1	Reference	-	-	Reference	-	-
D2	4.066	0.421-39.278	0.225			
Lymph node metastasis	1.813	0.390-3.871	0.003	2.126	0.002-13.266	0.031
Residual tumor	5.160	2.391-9.107	0.021	4.275	1.049-27.420	0.043

HR: Hazard ratio; CI: Confidence interval.

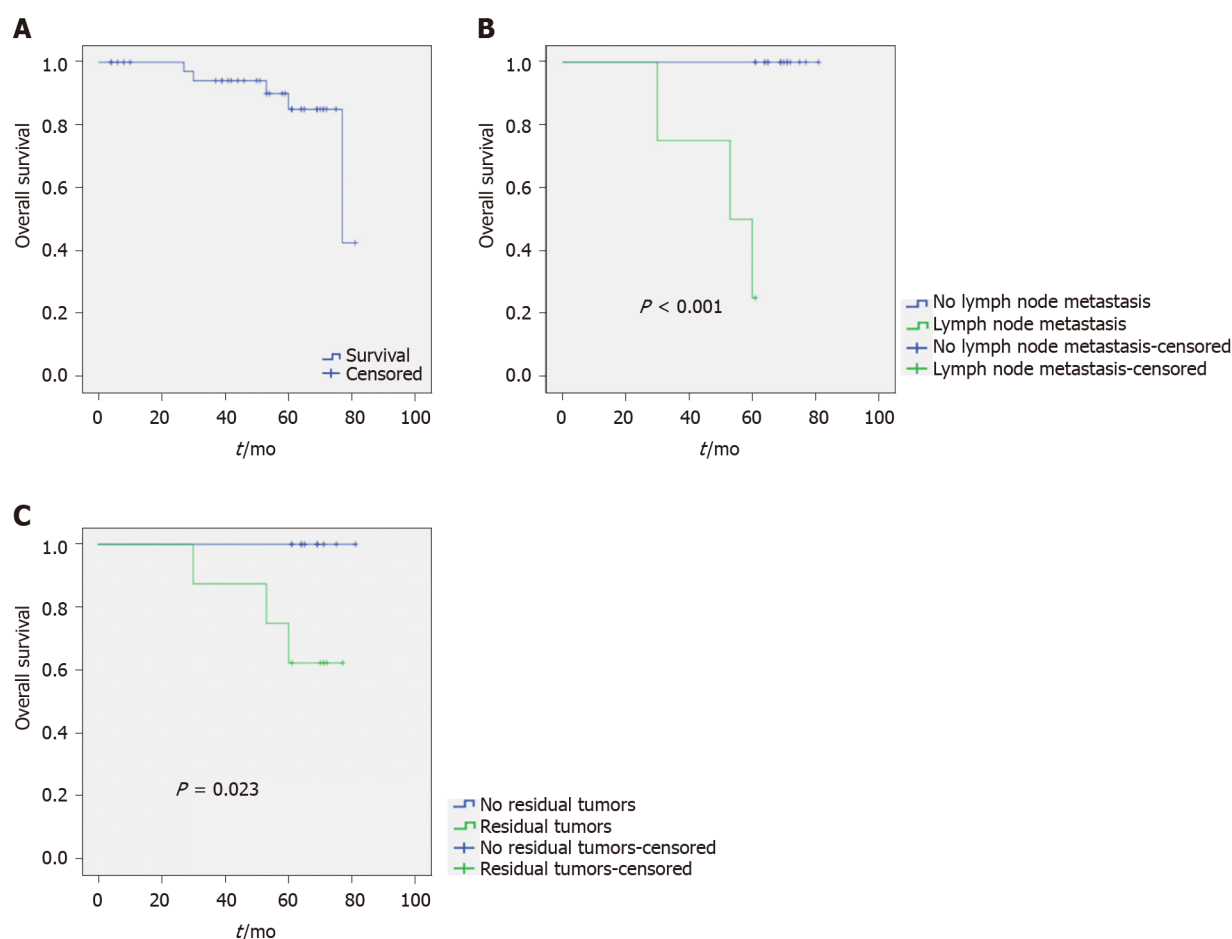


Figure 1 Overall survival of patients with early gastric cancer. A: All patients. Overall survival (OS), 77.0 ± 12.1 mo [95% confidence interval (CI): 53.3-100.7]; 3-yr OS rate, 94.1%; 5-yr OS rate, 85%; B: Lymph node metastasis vs none. $P < 0.001$. Lymph node metastasis group: OS, 69.0 ± 2.7 mo (95%CI: 63.7-74.3); 3-yr OS rate, 60%; 5-yr OS rate, 25%; C: Residual tumor vs none. $P = 0.023$. Residual tumor group: 3-yr OS rate, 80%; 5-yr OS rate, 62.5%.

there was a statistically significant difference in the survival *vs* those without residual tumor ($P = 0.023$) (Figure 1C). A total of 34 patients were followed for 3 years. The 3-year OS rate of patients with residual tumor was 80%, and that of patients without residual tumor was 100%. A total of 20 patients were followed for 5 years. The 5-year OS rate of patients without residual tumor was significantly higher than that of patients with residual tumor.

DISCUSSION

At present, for EGC patients who underwent non-curative ESD, surgeons need to comprehensively assess the risks of lymph node metastasis and residual tumor to determine the potential benefits of additional surgery^[24] in order to keep surgical trauma as low as possible while maximizing prognosis. Achieving the best balance between radical surgery for EGC and surgical trauma remains an unresolved issue. This study aimed to examine the impacts of lymph node metastasis and residual tumor on long-term prognosis, as well as risk factors for OS after additional surgery in patients with EGC who initially underwent ESD. The results indicated that male sex, T1b invasion, undifferentiated tumor, lymph node metastasis, and residual tumor were independently associated with OS in patients with EGC who underwent additional surgery after ESD.

Lymph node metastasis is one of the most important factors affecting the prognosis of patients with cancer in general, including EGC, and has a direct impact on the selection of the treatment method^[6,7]. Due to the low positive lymph node rate in EGC, many patients undergo unnecessary lymph node dissection or radical surgery, resulting in increased morbidity. Therefore, in order to effectively evaluate the risk of lymph node metastasis in patients who underwent non-curative ESD, multiple studies performed in Japan, South Korea, and Western countries reported rates of lymph node metastasis in EGC patients undergoing additional surgery after ESD of 4.3%-12.7%^[25-28]. In the present study, lymph node metastasis occurred in five of the 42 patients with EGC, reflecting a metastasis rate of 11.9%, corroborating previous studies. Ryu *et al.*^[29] showed that in 1076 patients with EGC, the rate of lymph node metastasis was lower in male patients than in females, *i.e.*, 7.8% *vs* 12.9%. In the latter report, multivariable analysis revealed that in female patients, invasion depth and vascular invasion were independent risk factors for lymph node metastasis. Compared with male patients, females were prone to developing lymph node metastasis, which may be due to the differences of molecular biological characteristics of EGC in different genders. Second, it may be related to differences in the hormonal regulatory system *in vivo*, but the specific mechanism needs further investigation. Meanwhile, large-scale studies of EGC patients with tumor invasion to T1b-SM2 showed that undifferentiated tumor is an independent prognostic factor of lymph node metastasis in case of tumor invasion into the submucosa^[30,31]. Previous findings also suggested that vascular invasion, nerve invasion, tumor size, positive margin, and general type are high-risk factors for lymph node metastasis in EGC^[15,23,25,32-34]. In the present study, the number of patients with lymph node metastasis was too small to determine the exact factors associated. However, lymph node metastasis was independently associated with OS in patients with EGC in this study. In addition, male sex, deeper tumor invasion, and undifferentiated histological type were all independent risk factors for OS.

Nevertheless, in patients undergoing non-curative resection, the rate of lymph node metastasis was not high; in such cases, a simple follow-up could be considered instead of additional surgery. Indeed, additional surgery after ESD increases the risk of surgical complications and morbidity, and there is also the possibility of no residual cancer in pathological tissue specimens after radical surgery^[35]. Therefore, developing an accurate model for assessing lymph node metastasis and tumor recurrence to reduce unnecessary surgery remains a hot topic. Hatta *et al.*^[23] evaluated 1101 EGC patients who underwent additional surgery after ESD and proposed the “eCura scoring system”, demonstrating lymph node metastasis rates in the low-risk, moderate-risk, and high-risk groups of 2.5%, 6.7%, 22.7%, respectively. In a subsequent multicenter study^[36], authors found that in high-risk group patients according to the “eCura scoring system”, the simple observation group had a higher tumor recurrence rate compared with the additional surgery group (HR = 3.13, *P* = 0.024). In the present study, the 3- and 5-year OS rates in patients without lymph node metastasis were significantly higher than those of patients with lymph node metastasis, partly confirming that lymph node metastasis affects the long-term prognosis of patients with EGC. Another study by Hatta *et al.*^[37] showed that in patients with EGC and lymph node metastasis or vascular invasion, even if additional radical surgery is performed after ESD, there is still a high risk of recurrence, and adjuvant chemotherapy might be considered. Therefore, in patients with EGC and lymph node metastasis, adjuvant chemotherapy should be performed at the same time according to each patient's specific conditions to improve the prognosis while performing additional radical surgery.

In addition, the depth of invasion was independently associated with OS. Deeper tumors have a higher likelihood of leaving cancer cells in place and subsequently

increase the risk of residual tumor, adversely affecting prognosis. Sekiguchi *et al*^[38] conducted a postoperative follow-up of 77 patients after ESD with a positive horizontal resection margin, and found that 11.9% had tumor recurrence after surgery, with a 5-year OS rate of 94.2%. Suzuki *et al*^[26] reported that in patients who underwent non-curative resection after ESD, the 5-year OS rates in the additional surgery and the observation groups were 91.0% and 75.5%, respectively ($P < 0.0001$), and the disease-specific survival rates were 99% and 96.8%, respectively ($P = 0.01$). Yano *et al*^[20] found that the prognosis of patients with additional surgery after non-curative ESD was significantly better than that of patients without, and the 5-year OS rates were 96% and 73.3%, respectively. In this study, the 3- and 5-year OS rates of patients with residual tumor were 80% and 62.5%, respectively, which were significantly lower than those of cases without residual tumor ($P < 0.05$). Therefore, in patients with potential residual tumor or non-curative resection, additional surgery could benefit survival to a certain extent. In addition, consistent with the above results, an undifferentiated tumor is also associated with OS^[8,12,14,18,39].

This study had some limitations, mainly as a retrospective, single-center study. Although the proportion of EGC among all GCs has increased in recent years in China compared with Japan, South Korea, and other countries, the detection rate of EGC in the Chinese population remains low, leading to a small sample size for patients undergoing additional radical surgery after ESD. Thus, biases may be present in the analysis of clinical data. Consequently, large-sample, multicenter clinical studies are still needed for confirmation.

CONCLUSION

In conclusion, male sex, T1b invasion, undifferentiated tumor, lymph node metastasis, and residual tumor were independently associated with OS in patients with EGC who underwent additional surgery after ESD. The long-term survival rate of patients with EGC but without lymph node metastasis and no residual tumor is significantly higher than that of those with lymph node metastasis and residual tumor. Therefore, in some patients with EGC, ESD could be considered a safe and effective treatment. Nevertheless, additional radical surgery must be considered on a case-by-case basis in order to maximize the radical resection of the tumor and improve long-term prognosis.

ARTICLE HIGHLIGHTS

Research background

Controversy exists about the benefit of additional surgery after endoscopic submucosal dissection (ESD) for early gastric cancer (EGC).

Research motivation

Whether patients who do not meet the criteria for curative resection after ESD need further surgery remains largely controversial. Therefore, factors associated with patient prognosis should be identified, which would provide predictive tools for clinical decisions.

Research objectives

This study aimed to assess the risk factors for overall survival (OS) upon additional surgery in patients with EGC who initially underwent ESD, especially the impacts of lymph node metastasis and residual tumor.

Research methods

Patients were retrospectively assessed, evaluating OS as the primary outcome, and lymph node metastasis and residual tumor as secondary outcomes. Logistic regression models and Kaplan-Meier curves were used for further analysis.

Research results

Male sex, T1b invasion, undifferentiated tumor, lymph node metastasis, and residual tumor were independently associated with OS. In the 4-81-mo follow-up period, OS was 77.0 ± 12.1 mo, and the 3-year and 5-year OS rates were 94.1% and 85%,

respectively.

Research conclusions

Male sex, T1b invasion, undifferentiated tumor, lymph node metastasis, and residual tumor are independently associated with OS in patients with EGC undergoing additional surgery after ESD.

Research perspectives

Compared with surgery, ESD could be a safe and effective treatment for some EGC patients to some extent. Nevertheless, additional radical surgery must be considered on a case-by-case basis in order to maximize the radical resection of the tumor and improve long-term prognosis.

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REFERENCES

- 1 Van Cutsem E, Sagaert X, Topal B, Haustermans K, Prenen H. Gastric cancer. *Lancet* 2016; **388**: 2654-2664 [PMID: 27156933 DOI: 10.1016/S0140-6736(16)30354-3]
- 2 Smyth EC, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D; ESMO Guidelines Committee. Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2016; **27**: v38-v49 [PMID: 27664260 DOI: 10.1093/annonc/mdw350]
- 3 Anderson WF, Camargo MC, Fraumeni JF Jr, Correa P, Rosenberg PS, Rabkin CS. Age-specific trends in incidence of noncardia gastric cancer in US adults. *JAMA* 2010; **303**: 1723-1728 [PMID: 20442388 DOI: 10.1001/jama.2010.496]
- 4 Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018; **68**: 394-424 [PMID: 30207593 DOI: 10.3322/caac.21492]
- 5 Wang Y, Li Z, Shan F, Miao R, Xue K, Li Z, Gao C, Chen N, Gao X, Li S, Ji J. [Current status of diagnosis and treatment of early gastric cancer in China--Data from China Gastrointestinal Cancer Surgery Union]. *Zhonghua Wei Chang Wai Ke Za Zhi* 2018; **21**: 168-174 [PMID: 29492915]
- 6 NCCN E. NCCN Clinical Practice Guidelines in Oncology. Gastric cancer: official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association. 2007: 1. Available from: http://www.nccn.org/professionals/physician_gls/default.aspx
- 7 Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018 (5th edition). *Gastric Cancer* 2021; **24**: 1-21 [PMID: 32060757 DOI: 10.1007/s10120-020-01042-y]
- 8 Bang CS, Park JM, Baik GH, Park JJ, Joo MK, Jang JY, Jeon SW, Choi SC, Sung JK, Cho KB. Therapeutic Outcomes of Endoscopic Resection of Early Gastric Cancer with Undifferentiated-Type Histology: A Korean ESD Registry Database Analysis. *Clin Endosc* 2017; **50**: 569-577 [PMID: 28743132 DOI: 10.5946/ce.2017.017]
- 9 Nishizawa T, Yahagi N. Long-Term Outcomes of Using Endoscopic Submucosal Dissection to Treat Early Gastric Cancer. *Gut Liver* 2018; **12**: 119-124 [PMID: 28673068 DOI: 10.5009/gnl17095]
- 10 Tanabe S, Ishido K, Matsumoto T, Kosaka T, Oda I, Suzuki H, Fujisaki J, Ono H, Kawata N, Oyama T, Takahashi A, Doyama H, Kobayashi M, Uedo N, Hamada K, Toyonaga T, Kawara F, Tanaka S, Yoshifuku Y. Long-term outcomes of endoscopic submucosal dissection for early gastric cancer: a multicenter collaborative study. *Gastric Cancer* 2017; **20**: 45-52 [PMID: 27807641 DOI: 10.1007/s10120-016-0664-7]
- 11 Rong L, Cai Y, Nian W, Wang X, Liang J, He Y, Zhang J. [Efficacy comparison between surgical resection and endoscopic submucosal dissection of early gastric cancer in a domestic single center]. *Zhonghua Wei Chang Wai Ke Za Zhi* 2018; **21**: 190-195 [PMID: 29492919]
- 12 Zhu ZL, Shi HP, Beecharry MK, Feng TN, Yan M, Yuan F, Zheng-Gang Zhu, Zhang BY, Wu W. Expanding the indication of endoscopic submucosal dissection for undifferentiated early gastric cancer is safe or not? *Asian J Surg* 2020; **43**: 526-531 [PMID: 31706922 DOI: 10.1016/j.asjsur.2019.08.006]
- 13 Hatta W, Gotoda T, Oyama T, Kawata N, Takahashi A, Yoshifuku Y, Hoteya S, Nakamura K, Hirano M, Esaki M, Matsuda M, Ohnita K, Shimoda R, Yoshida M, Dohi O, Takada J, Tanaka K, Yamada S, Tsuji T, Ito H, Hayashi Y, Nakamura T, Shimosegawa T. Is radical surgery necessary in all patients who do not meet the curative criteria for endoscopic submucosal dissection in early gastric cancer? *J Gastroenterol* 2017; **52**: 175-184 [PMID: 27098174 DOI: 10.1007/s00535-016-1210-4]
- 14 Kim HW, Kim JH, Park JC, Jeon MY, Lee YC, Lee SK, Shin SK, Chung HS, Noh SH, Kim JW, Choi SH, Park JJ, Youn YH, Park H. Additive endoscopic resection may be sufficient for patients

- with a positive lateral margin after endoscopic resection of early gastric cancer. *Gastrointest Endosc* 2017; **86**: 849-856 [PMID: [28288840](#) DOI: [10.1016/j.gie.2017.02.037](#)]
- 15 **Akaike H**, Kawaguchi Y, Shiraishi K, Shimizu H, Furuya S, Hosomura N, Amemiya H, Kawaida H, Sudoh M, Inoue S, Kohno H, Ichikawa D. Validity of additional surgical resection by comparing the operative risk with the stratified lymph node metastatic risk in patients with early gastric cancer after endoscopic submucosal dissection. *World J Surg Oncol* 2019; **17**: 136 [PMID: [31382963](#) DOI: [10.1186/s12957-019-1679-4](#)]
 - 16 **Pyo JH**, Lee H, Min BH, Lee JH, Choi MG, Lee JH, Sohn TS, Bae JM, Kim KM, Ahn JH, Carriere KC, Kim JJ, Kim S. Long-Term Outcome of Endoscopic Resection vs. Surgery for Early Gastric Cancer: A Non-inferiority-Matched Cohort Study. *Am J Gastroenterol* 2016; **111**: 240-249 [PMID: [26782817](#) DOI: [10.1038/ajg.2015.427](#)]
 - 17 **Jung DH**, Lee YC, Kim JH, Lee SK, Shin SK, Park JC, Chung H, Park JJ, Youn YH, Park H. Additive treatment improves survival in elderly patients after non-curative endoscopic resection for early gastric cancer. *Surg Endosc* 2017; **31**: 1376-1382 [PMID: [27450206](#) DOI: [10.1007/s00464-016-5123-3](#)]
 - 18 **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](#)]
 - 19 **Hasuike N**, Ono H, Boku N, Mizusawa J, Takizawa K, Fukuda H, Oda I, Doyama H, Kaneko K, Hori S, Iishi H, Kurokawa Y, Muto M; Gastrointestinal Endoscopy Group of Japan Clinical Oncology Group (JCOG-GIESG). A non-randomized confirmatory trial of an expanded indication for endoscopic submucosal dissection for intestinal-type gastric cancer (cT1a): the Japan Clinical Oncology Group study (JCOG0607). *Gastric Cancer* 2018; **21**: 114-123 [PMID: [28224238](#) DOI: [10.1007/s10120-017-0704-y](#)]
 - 20 **Yano T**, Ishido K, Tanabe S, Wada T, Azuma M, Kawanishi N, Yamane S, Watanabe A, Katada C, Koizumi W. Long-term outcomes of patients with early gastric cancer found to have lesions for which endoscopic treatment is not indicated on histopathological evaluation after endoscopic submucosal dissection. *Surg Endosc* 2018; **32**: 1314-1323 [PMID: [28840337](#) DOI: [10.1007/s00464-017-5809-1](#)]
 - 21 **Conlin A**, Kaltenbach T, Kusano C, Matsuda T, Oda I, Gotoda T. Endoscopic resection of gastrointestinal lesions: advancement in the application of endoscopic submucosal dissection. *J Gastroenterol Hepatol* 2010; **25**: 1348-1357 [PMID: [20659223](#) DOI: [10.1111/j.1440-1746.2010.06402.x](#)]
 - 22 **Gotoda T**, Yamamoto H, Soetikno RM. Endoscopic submucosal dissection of early gastric cancer. *J Gastroenterol* 2006; **41**: 929-942 [PMID: [17096062](#) DOI: [10.1007/s00535-006-1954-3](#)]
 - 23 **Hatta W**, Gotoda T, Oyama T, Kawata N, Takahashi A, Yoshifuku Y, Hoteya S, Nakagawa M, Hirano M, Esaki M, Matsuda M, Ohnita K, Yamanouchi K, Yoshida M, Dohi O, Takada J, Tanaka K, Yamada S, Tsuji T, Ito H, Hayashi Y, Nakaya N, Nakamura T, Shimosegawa T. A Scoring System to Stratify Curability after Endoscopic Submucosal Dissection for Early Gastric Cancer: "eCura system". *Am J Gastroenterol* 2017; **112**: 874-881 [PMID: [28397873](#) DOI: [10.1038/ajg.2017.95](#)]
 - 24 **Ono H**, Yao K, Fujishiro M, Oda I, Nimura S, Yahagi N, Iishi H, Oka M, Ajioka Y, Ichinose M, Matsui T. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. *Dig Endosc* 2016; **28**: 3-15 [PMID: [26234303](#) DOI: [10.1111/den.12518](#)]
 - 25 **Jung DH**, Huh CW, Kim JH, Hong JH, Park JC, Lee YC, Youn YH, Park H, Choi SH, Noh SH. Risk-Stratification Model Based on Lymph Node Metastasis After Noncurative Endoscopic Resection for Early Gastric Cancer. *Ann Surg Oncol* 2017; **24**: 1643-1649 [PMID: [28150166](#) DOI: [10.1245/s10434-017-5791-9](#)]
 - 26 **Suzuki H**, Oda I, Abe S, Sekiguchi M, Nonaka S, Yoshinaga S, Saito Y, Fukagawa T, Katai H. Clinical outcomes of early gastric cancer patients after noncurative endoscopic submucosal dissection in a large consecutive patient series. *Gastric Cancer* 2017; **20**: 679-689 [PMID: [27722825](#) DOI: [10.1007/s10120-016-0651-z](#)]
 - 27 **Kim ER**, Lee H, Min BH, Lee JH, Rhee PL, Kim JJ, Kim KM, Kim S. Effect of rescue surgery after non-curative endoscopic resection of early gastric cancer. *Br J Surg* 2015; **102**: 1394-1401 [PMID: [26313295](#) DOI: [10.1002/bjs.9873](#)]
 - 28 **Probst A**, Schneider A, Schaller T, Anthuber M, Ebigo A, Messmann H. Endoscopic submucosal dissection for early gastric cancer: are expanded resection criteria safe for Western patients? *Endoscopy* 2017; **49**: 855-865 [PMID: [28564714](#) DOI: [10.1055/s-0043-110672](#)]
 - 29 **Ryu ES**, Chang SJ, An J, Yang JY, Chung JW, Kim YJ, Kim KO, Park DK, Kwon KA, Nam S, Lee WK, Kim JH. Sex-specific differences in risk factors of lymph node metastasis in patients with early gastric cancer. *PLoS One* 2019; **14**: e0224019 [PMID: [31626653](#) DOI: [10.1371/journal.pone.0224019](#)]
 - 30 **Liang XQ**, Wang Z, Li HT, Ma G, Yu WW, Zhou HC, Liu HB. Indication for endoscopic treatment based on the risk of lymph node metastasis in patients with undifferentiated early gastric cancer. *Asian J Surg* 2020; **43**: 973-977 [PMID: [31964584](#) DOI: [10.1016/j.asjsur.2019.12.002](#)]
 - 31 **Miyahara K**, Hatta W, Nakagawa M, Oyama T, Kawata N, Takahashi A, Yoshifuku Y, Hoteya S, Hirano M, Esaki M, Matsuda M, Ohnita K, Shimoda R, Yoshida M, Dohi O, Takada J, Tanaka K, Yamada S, Tsuji T, Ito H, Aoyagi H, Shimosegawa T. The Role of an Undifferentiated Component in Submucosal Invasion and Submucosal Invasion Depth After Endoscopic Submucosal Dissection for Early Gastric Cancer. *Digestion* 2018; **98**: 161-168 [PMID: [29870985](#) DOI: [10.1159/000488529](#)]

- 32 **Zhao B**, Zhang J, Zhang J, Luo R, Wang Z, Xu H, Huang B. Risk Factors Associated with Lymph Node Metastasis for Early Gastric Cancer Patients Who Underwent Non-curative Endoscopic Resection: a Systematic Review and Meta-analysis. *J Gastrointest Surg* 2019; **23**: 1318-1328 [PMID: 30187319 DOI: 10.1007/s11605-018-3924-5]
- 33 **Du MZ**, Gan WJ, Yu J, Liu W, Zhan SH, Huang S, Huang RP, Guo LC, Huang Q. Risk factors of lymph node metastasis in 734 early gastric carcinoma radical resections in a Chinese population. *J Dig Dis* 2018; **19**: 586-595 [PMID: 30207084 DOI: 10.1111/1751-2980.12670]
- 34 **Sunagawa H**, Kinoshita T, Kaito A, Shibasaki H, Kaneko K, Ochiai A, Ohtsu A, Nishida T. Additional surgery for non-curative resection after endoscopic submucosal dissection for gastric cancer: a retrospective analysis of 200 cases. *Surg Today* 2017; **47**: 202-209 [PMID: 27194020 DOI: 10.1007/s00595-016-1353-1]
- 35 **Nakata B**, Tendo M, Okuyama M, Nakahara K, Ishizu H, Masuda G, Lee T, Hori T, Ohsawa M, Sato H, Ishikawa T. Additional surgical resection after endoscopic mucosal dissection for early gastric cancer: A medium-sized hospital's experience. *Int J Surg* 2016; **36**: 335-341 [PMID: 27871804 DOI: 10.1016/j.ijssu.2016.11.084]
- 36 **Hatta W**, Gotoda T, Oyama T, Kawata N, Takahashi A, Yoshifuku Y, Hoteya S, Nakagawa M, Hirano M, Esaki M, Matsuda M, Ohnita K, Yamanouchi K, Yoshida M, Dohi O, Takada J, Tanaka K, Yamada S, Tsuji T, Ito H, Hayashi Y, Nakamura T, Nakaya N, Shimosegawa T. Is the eCura system useful for selecting patients who require radical surgery after noncurative endoscopic submucosal dissection for early gastric cancer? *Gastric Cancer* 2018; **21**: 481-489 [PMID: 28983696 DOI: 10.1007/s10120-017-0769-7]
- 37 **Hatta W**, Gotoda T, Oyama T, Kawata N, Takahashi A, Oka S, Hoteya S, Nakagawa M, Hirano M, Esaki M, Matsuda M, Ohnita K, Shimoda R, Yoshida M, Dohi O, Takada J, Tanaka K, Yamada S, Tsuji T, Ito H, Aoyagi H, Nakamura T, Nakaya N, Shimosegawa T, Masamune A. Is Additional Surgery Always Sufficient for Preventing Recurrence After Endoscopic Submucosal Dissection with Curability C-2 for Early Gastric Cancer? *Ann Surg Oncol* 2019; **26**: 3636-3643 [PMID: 31342376 DOI: 10.1245/s10434-019-07579-2]
- 38 **Sekiguchi M**, Suzuki H, Oda I, Abe S, Nonaka S, Yoshinaga S, Taniguchi H, Sekine S, Kushima R, Saito Y. Risk of recurrent gastric cancer after endoscopic resection with a positive lateral margin. *Endoscopy* 2014; **46**: 273-278 [PMID: 24505020 DOI: 10.1055/s-0034-1364938]
- 39 **Li D**, Luan H, Wang S, Zhou Y. Survival benefits of additional surgery after non-curative endoscopic resection in patients with early gastric cancer: a meta-analysis. *Surg Endosc* 2019; **33**: 711-716 [PMID: 30397744 DOI: 10.1007/s00464-018-6570-9]



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