J Gastric Cancer. 2025 Jan;25(1):210-227
https://doi.org/10.5230/jgc.2025.25.e5
pISSN 2093-582X·eISSN 2093-5641

Journal of Gastric Cancer

Review Article

Check for updates

Management Strategy of Non-curative ESD in Gastric Cancer: Curative Criteria, and the Critical Building Block for Determining Beyond It

Hyuk Lee

Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

OPEN ACCESS

Received: Oct 26, 2024
Revised: Dec 7, 2024
Accepted: Dec 7, 2024
Published online: Dec 24, 2024

Correspondence to
Hyuk Lee
Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Korea.
Email: leehyuk@skku.edu

Copyright © 2025. Korean Gastric Cancer Association
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs
Hyuk Lee
https://orcid.org/0000-0003-4271-7205

Funding
This research was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: RS-2024-004370388).

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

ABSTRACT

Endoscopic submucosal dissection is performed in cases of early gastric cancer, where the risk of lymph node metastasis (LNM) is expected to be negligible, and 12%–21% of these patients are deemed to have undergone non-curative resections based on pathological criteria. In such cases, decisions regarding additional treatments must be made to maximize curability, depending on the anticipated LNM risk. Well-established risk factors for LNM include lymphatic invasion, vascular invasion, deep submucosal invasion, positive vertical margins, and larger tumor size. When pathological factors associated with a clear LNM risk, such as lymphatic or deep submucosal invasion, are present, additional gastrectomy with lymph node dissection should be considered. Conversely, in cases involving only a positive horizontal margin, additional endoscopic treatment may be an effective therapeutic option as opposed to gastrectomy because of the negligible risk of LNM despite the potential risk of residual tumors. Endoscopic resection is particularly advantageous for determining complete resection. In addition to pathological curability, patient-specific factors, such as age and comorbidities, must be considered. Several retrospective cohort studies have shown that the cause of mortality among patients placed only on observation without additional treatment after non-curative resection is generally related to underlying conditions irrelevant to gastric cancer. Thus, it is crucial to assess both GC-specific mortality and all-cause mortality to finalize treatment decisions that help minimize such mortality. Therefore, new treatment algorithms that integrate pathological curability with patient-specific factors must be developed.

Keywords: Stomach cancer; Endoscopic submucosal dissection; Treatment outcome; Gastrectomy

INTRODUCTION

Gastric cancer remains the fourth leading cause of cancer-related death worldwide. However, its mortality has significantly declined because of aggressive screening programs and the eradication of *Helicobacter pylori* infection. In addition to such a downward trend in mortality, the diagnosis of gastric cancer at an early stage has enabled the significantly more frequent use of endoscopic resection, especially endoscopic submucosal dissection (ESD), when appropriate indications are met. Therefore, ESD is now acknowledged as a common

Generated by XmlInkpress

jgc Journal of Gastric Cancer

treatment modality for early gastric cancer (EGC) [1-8]. However, ESD should be limited to cases in which the risk of lymph node metastasis (LNM) is negligible, necessitating a thorough post-ESD pathological evaluation to estimate the risk and consider other rescue therapies if the pathological curability criteria are not met [9]. Thus, the pathological curability criteria to identify non-curative resection following ESD are important, and they are crucial to guide further treatment depending on the specific pathological parameters of the criteria for non-curative resection. In addition, patient-related factors must be considered when making treatment decisions [10]. Interest in therapeutic strategies for managing non-curative ESD has been growing, particularly owing to the high incidence of upfront ESD in older adults or patients with severe comorbidities related to perioperative risks associated with gastrectomy [11]. This review aimed to summarize the key pathological criteria for determining non-curative resection after ESD, explore appropriate treatment modalities for non-curative resection, and review the implementation of treatment strategies considering patient-related factors and lesion characteristics.

DECISION FOR NON-CURATIVE RESECTION FOLLOWING ESD FOR EGC BASED ON PATHOLOGICAL CURATIVE CRITERIA

Curative resection following ESD is defined as the absence of tumor involvement in the horizontal or vertical resection margins, lymphovascular invasion, or complete resection of lesions that meet the absolute or expanded indications. Lesions that meet the absolute or expanded indications include the following: 1) differentiated intramucosal carcinoma without ulceration, regardless of tumor diameter; 2) differentiated intramucosal carcinoma with ulceration, with a tumor diameter of ≤3 cm; 3) differentiated submucosal carcinoma with an invasion depth of <500 μm, with a tumor diameter of ≤3 cm; and 4) undifferentiated intramucosal carcinoma without ulceration, with a tumor diameter of ≤3 cm. Lesions that do not meet these criteria are considered non-curative [2,12].

The criteria for non-curative resection proposed by traditional guidelines do not account for the differences between the various factors contributing to non-curative status. Recently, the Japanese guidelines introduced the e-Cura system, which categorizes the non-curative resection group (e-CuraC group) into e-CuraC-1 and e-CuraC-2. Tailored recommendations for additional treatment were provided for the 2 groups in response to different long-term outcome risks [13,14]. In practice, the rate of non-curative resection following ESD ranges from 12% to 21% across facilities, depending on their preference for performing upfront ESD or adopting a more conservative approach for case selection. For example, a multicenter study in Korea reported a non-curative resection rate of 21.4% (661 cases) in 3,094 ESD cases. Similarly, a prospective cohort study analyzing outcomes from 41 facilities in Japan using a web registry system reported a non-curative resection rate of 20.0% [15,16].

NATURAL COURSE OF EGC AFTER NON-CURATIVE ESD FOLLOWED BY NO ADDITIONAL TREATMENT

In cases where additional treatment is required following non-curative endoscopic resection but high-risk perioperative morbidity is anticipated due to comorbidities, observation may

https://doi.org/10.5230/jgc.2025.25.e5

jgc Journal of Gastric Cancer

be chosen over additional gastrectomy with lymph node dissection. However, long-term follow-up data on the natural course of untreated non-curative resection remain limited. Some studies have explored the clinical outcomes of patients with differentiated EGC who underwent non-curative resection and were followed up without additional rescue treatment. One study with a median follow-up period of 33 months reported a 25.2% mortality rate, with 85% of deaths attributed to causes unrelated to gastric cancer, and underlying disease was identified as a key factor linked to mortality [17]. Another study of patients with submucosal invasive cancer who underwent non-curative resection and were placed on long-term follow-up without additional treatment reported a cancer recurrence rate of 9.6%. In this study, mortality due to non-cancer-related causes was significantly higher than that due to gastric-cancer-specific causes (13.5% vs. 1.9%) [18]. In contrast, a study analyzing the long-term outcomes of 512 patients who underwent non-curative resection found that among 198 patients who were observed without additional treatment, cancer-specific survival and disease-free survival were significantly worse than those who underwent gastrectomy [19]. A long-term follow-up study from Japan reported that while gastric cancer-related deaths did not significantly increase in patients who did not receive additional treatment, the mortality rate due to other underlying diseases was significantly higher. This increase is attributed to the nature of these patients, who were unable to undergo surgical treatment because of their underlying conditions [20].

The long-term outcomes of patients placed under observation without additional treatment following non-curative resection are subject to selection bias, as they were obtained from retrospective cohort studies. These mixed results reflect the varying impacts of different causes of non-curative resection on long-term prognosis. For instance, the prognosis of patients who undergo non-curative resection due to lateral margin involvement differs significantly from that of patients with lymphovascular invasion. Hence, outcomes differed according to the composition of the patient cohort. To address these differences, the eCura system was introduced to stratify the risk of non-curative ESD cases based on the eCura score. The low- and intermediate-risk groups did not show better overall survival rates after observation than after surgery. However, in high-risk groups, the 5-year overall survival and recurrence-free survival rates were significantly lower in the observation group [21]. A study analyzing the timing of recurrence in patients under observation after non-curative resection reported that early recurrence (within 2 years) was associated with lymphatic invasion, whereas late recurrence (after 2 years) was linked to venous invasion. This suggests that treatment planning should consider life expectancy and the likelihood of recurrence in each patient [22].

Among patients who showed positive horizontal margin involvement and were under long-term follow-up without additional treatment, the local recurrence rate ranged from 11.9% to 25.9%, and local recurrence was associated with cancer-positive lateral margin length [23-26].

Figs. 1 and **2** illustrate cases of gastric cancer-related mortality, whereas **Fig. 3** shows a case of non-cancer-related mortality during long-term follow-up without additional treatment following non-curative ESD for EGC. **Fig. 4** presents a case of mortality due to non-gastric cancer in a patient who underwent gastrectomy after non-curative ESD.

https://doi.org/10.5230/jgc.2025.25.e5

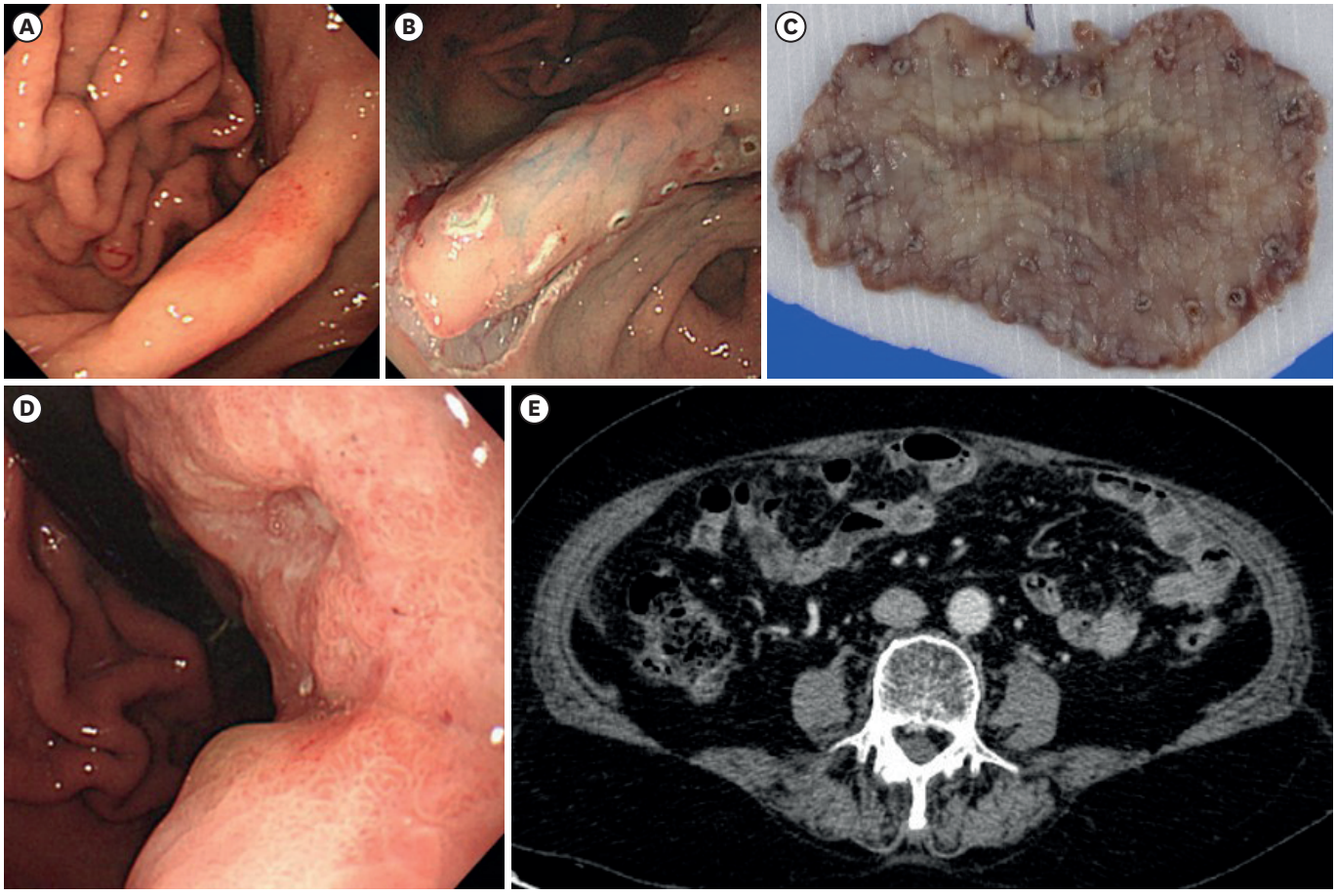

Fig. 1. Representative case of mortality in a patient with only follow-up after non-curative ESD. A 73-year-old female with a Charlson Comorbidity Index score of 0 underwent ESD for an early gastric cancer IIb + IIc lesion at an angle detected during esophagogastroduodenoscopy as part of a routine health checkup (A, B). Final pathology confirmed a 4.8 cm papillary adenocarcinoma with 200 μm submucosal and lymphatic invasion (C). Although the patient was in the intermediate-risk group for lymph node metastasis, she refused additional surgery. During follow-up, recurrent gastric cancer was detected at the ESD site after 40 months (D). Abdominal computed tomography showing peritoneal nodules and omental-mesenteric infiltrations compatible with peritoneal carcinomatosis (E). The patient received palliative chemotherapy but died 11 months later because of disease progression.
ESD = endoscopic submucosal dissection.

LNM RATE IN NON-CURATIVE ESD FOR EGC

Non-curative resection results from a single or combination of various pathological factors, such as tumor size, differentiated or undifferentiated cancer, submucosal invasion, presence of an ulcer, invasion of the horizontal or vertical resection margin, and presence of lymphovascular invasion. Thus, LNM rates in cases involving different factors are clinically important for treatment stratification. In a multicenter study, lymphatic invasion was identified as the most significant risk factor for LNM, followed by tumor size >30 mm, positive vertical margins, venous invasion, and deep submucosal invasion. Risk stratification was performed based on these risk factors, and the LNM rate ranged from 2.5% to 22.7% [13]. A meta-analysis of 24 studies involving 3,877 patients who underwent gastrectomy following non-curative ESD reported LNM rates ranging from 0% to 12%, with a pooled prevalence of 8.1%. These rates were similar across the countries in which the studies were conducted. One key conclusion of this meta-analysis was that the significant risk factors for LNM included lymphatic invasion, vascular invasion, deep submucosal invasion, positive vertical margins, and tumor size >30 mm. In contrast, patients with only positive horizontal

https://doi.org/10.5230/jgc.2025.25.e5

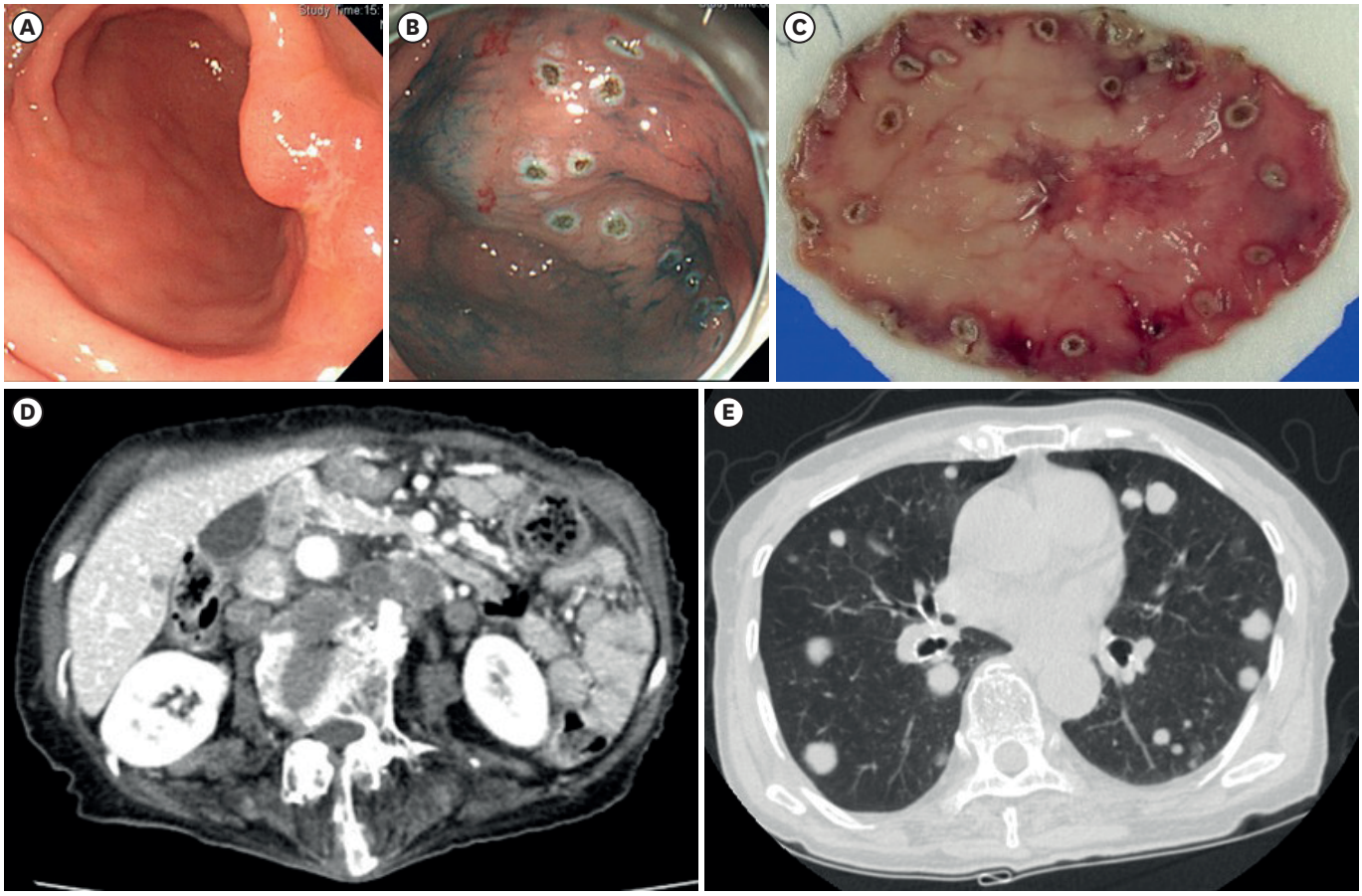

Fig. 2. Representative case of mortality in a patient with only follow-up after non-curative ESD. A 74-year-old female with a Charlson Comorbidity Index score of 0 underwent ESD for an early gastric cancer IIc + IIa lesion in the posterior antrum, which was discovered during esophagogastroduodenoscopy as part of a routine health checkup (A, B). Final pathology confirmed a 2.6 cm moderately differentiated tubular adenocarcinoma with 1,000 μm of submucosal invasion, lymphatic invasion, and positive vertical margin invasion (C). Despite being in the high-risk group for LNM, the patient refused additional surgery and was lost to follow-up. The patient returned 30 months post-ESD. Abdominal computed tomography revealed extensive LNM in the abdominopelvic cavity and metastatic soft tissue density in the iliac bifurcation and prevertebral body areas (D). Chest computed tomography showed metastatic lung nodules (E). The patient died 2 months later.
ESD = endoscopic submucosal dissection; LNM = lymph node metastasis.

margins showed negligible LNM risk. By demonstrating that LNM risk varies markedly between the e-CuraC-1 and e-CuraC-2 groups, this study substantiates the utility of the newly introduced e-Cura system [10]. A retrospective study in Korea that analyzed cases determined as non-curative resection based on factors other than lymphatic invasion, the most well-established risk factor for LNM, found an overall LNM rate of 7.1%, with tumor size greater than 3 cm, submucosal invasion, and undifferentiated cancer types being strongly associated with LNM [27]. In particular, the LNM risk associated with the undifferentiated type varies widely depending on various pathological criteria. For instance, while tumors <2 cm, without ulceration, and limited to the mucosa are considered indications for endoscopic resection, further stratification is required based on emerging pathological evidence [28,29]. Recent meta-analyses have also demonstrated that the LNM rate of mixed-type intramucosal undifferentiated cancers is higher (7.4%–7.8%) than that of pure undifferentiated EGC, suggesting that individualized approaches are needed to select additional treatments for mixed-type cases [30-34]. In a recent multicenter retrospective cohort study of undifferentiated-type EGC, analysis using the e-Cura system showed LNM rates of 2.6%, 10.9%, and 14.8% in the low-, intermediate-, and high-risk categories, respectively. Using a

https://doi.org/10.5230/jgc.2025.25.e5

jgc Journal of Gastric Cancer

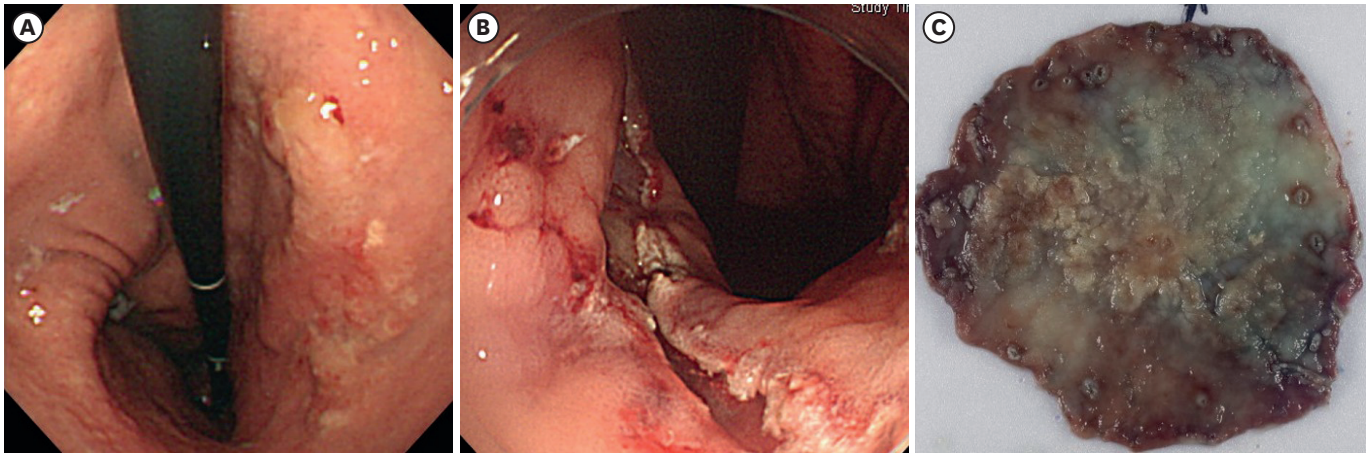

Fig. 3. Representative case of mortality in a patient with only follow-up after non-curative ESD. An 86-year-old male with a Charlson Comorbidity Index score of 3 underwent ESD for an early gastric cancer IIa + IIb lesion in the posterior lower body, which was discovered during esophagogastroduodenoscopy as part of a routine health checkup (A, B). Final pathology revealed a 6.4 cm moderately differentiated tubular adenocarcinoma with 2,400 μm submucosal and lymphatic invasion (C). The patient was in the high-risk group for lymph node metastasis but did not undergo additional surgery. The patient died 7 months after experiencing pneumonia with sepsis.
ESD = endoscopic submucosal dissection.

modified e-Cura system, the LNM rates were 1.1%, 5.4%, and 13.3%, respectively [35,36]. **Table 1** shows the LNM rates among patients who underwent gastrectomy following non-curative ESD across various studies.

CRITERIA-BASED TREATMENT STRATEGIES AFTER NON-CURATIVE ESD

Treatment plans can be established based on various results regarding LNM rates in EGC, whether primary surgery or additional surgery after non-curative ESD. Generally, gastrectomy with lymph node dissection is the standard rescue therapy [64]. In a propensity score matching analysis comparing patients who underwent ESD without an indication for ESD and were placed only on follow-up without additional surgery to those who underwent initial standard surgery, the former group showed significantly higher 5-year mortality (26.0% vs. 14.5%) and cancer recurrence rates (17.0% vs. 0), demonstrating that additional gastrectomy offers survival benefits in non-curative ESD [76]. Another study also showed that additional surgery after non-curative ESD for EGC significantly reduced gastric cancer-related death (hazard ratio, 0.33; 95% confidence interval, 0.12–0.79) [77]. Similarly, in an analysis of 341 non-curative ESD cases, the status of rescue surgery was an independent predictor of 5-year overall survival (hazard ratio, 0.43; 95% confidence interval, 0.18–1.00) [64]. **Table 2** lists studies comparing the effectiveness of additional treatment in non-curative ESD for EGC with observation groups.

However, it has been confirmed that the LNM rate varies according to several pathological risk factors involved in non-curative resection, and based on the e-Cura system that considers these factors, patients requiring gastrectomy are defined as a high-risk group [83]. In particular, guidelines have suggested that local treatment should be considered over gastrectomy in patients showing only positive horizontal resection margin involvement, given the negligible LNM rate in this patient group. Recent guidelines state that in cases where only positive horizontal resection margins are observed without other factors of non-

https://doi.org/10.5230/jgc.2025.25.e5

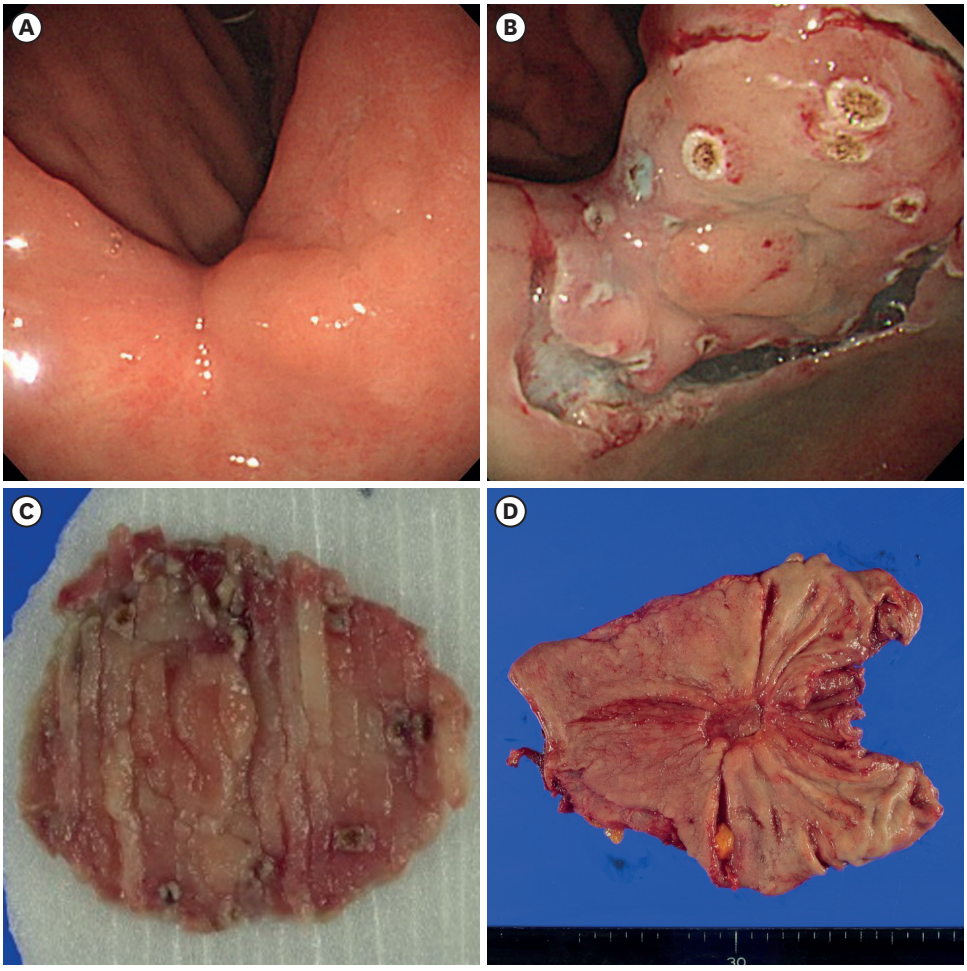

Fig. 4. Representative case of mortality in a patient with additional surgery after non-curative ESD. A 75-year-old male with a Charlson Comorbidity Index score of 3 underwent ESD for an early gastric cancer IIa + IIb lesion on the lesser curvature of the lower body, which was discovered during esophagogastroduodenoscopy as part of a routine health checkup (A, B). Final pathology revealed a 2.8 cm moderately differentiated intramucosal tubular adenocarcinoma with multiple positive lateral margin invasions (C). The patient was in the low-risk group; however, subtotal gastrectomies B-I were performed (D). A 2.5 cm residual intramucosal tumor was noted, but there was no evidence of lymph node metastasis. The patient died of hemorrhagic stroke 26 months postoperatively.
ESD = endoscopic submucosal dissection.

curative resection, repeated ESD can be an option in addition to gastrectomy, and careful follow-up without any special additional treatment has been proposed as a viable approach [2,12,14,92].

A multicenter survey of clinical approaches for patients with positive horizontal or indeterminable margins following ESD showed that only 42.8% of the patients underwent early intervention, whereas the rest were placed under observation. Among those who underwent early intervention, the most common treatment was ablation therapy through coagulation, followed by surgical resection or re-ESD, although the rates varied significantly across institutions. This suggests that treatment guidelines for managing positive horizontal or indeterminable margins after ESD are not well established [93]. Generally, patients with positive horizontal resection margins are not at significant risk of LNM but have a substantially higher likelihood of residual cancer. Therefore, additional resection, preferably

https://doi.org/10.5230/jgc.2025.25.e5

jgc Journal of Gastric Cancer

Table 1. LNM and local residual positive rates among patients who underwent gastrectomy following non-curative ESD for EGC

Author/Country	Year	Study design	Study population	No. of additional gastrectomy cases	LNM rate (%)	Local residual positive rate (%)
Morais et al./Multi-country in Europe [37]	2023	Multicenter, prospective cohort	High-risk NCR	156	14.7	25.0
Jin et al./China [38]	2023	Multicenter, retrospective cohort	NCR	68	4.4	11.8
Sun et al./China [39]	2023	Single-center, retrospective cohort	NCR	133	10.5	13.5
Park et al./Korea [40]	2022	Single-center, retrospective cohort	Surgical cases in the upper third with NCR criteria only, without ESD	379	9.5	-
Makimoto et al./Japan [41]	2022	Single-center, retrospective cohort	NCR	100	14.0	7.0
Kim et al./Korea [42]	2022	Single-center, retrospective cohort	Positive horizontal margin	45	2.2	71.1
Yang et al./Korea [43]	2021	Multicenter, retrospective cohort	NCR in undifferentiated-type	270	6.7	-
Yang et al./Korea [44]	2021	Multicenter, retrospective cohort	Positive horizontal margin in undifferentiated-type	40	0	65.0
Jeong et al./Korea [45]	2021	Single-center, retrospective cohort	NCR	73	8.2	9.6
Kang et al./Korea [46]	2020	Single-center, retrospective cohort	NCR	140	12.1	-
Tian et al./China [47]	2019	Single-center, retrospective cohort	NCR	45	11.1	22.2
Kim et al./Korea [48]	2019	Single-center, retrospective cohort	NCR	113	13.3	20.4
Suzuki et al./Japan [49]	2019	Multicenter, prospective cohort	NCR	824	7.8	7.4
Yano et al./Japan [50]	2018	Single-center, retrospective cohort	NCR	118	10.2	-
Jung et al./Korea [51]	2017	Multicenter, retrospective cohort	NCR	321	7.2	13.4
Toya et al./Japan [52]	2017	Single-center, retrospective cohort	NCR with R0 resection	45	2.2	2.2
Suzuki et al./Japan [53]	2017	Single-center, retrospective cohort	NCR, except for the positive horizontal margin	356	5.1	-
Probst et al./Germany [54]	2017	Single-center, prospective cohort	NCR	12	8.3	0
Kim et al./Korea [55]	2017	Single-center, retrospective cohort	NCR	350	8.6	20.9
Goto et al./Japan [56]	2017	Single-center, retrospective cohort	NCR	73	11.0	-
Sunagawa et al./Japan [57]	2017	Single-center, retrospective cohort	NCR	200	7.5	11.5
Kim et al./Korea [58]	2017	Single-center, retrospective cohort	Positive horizontal margin	28	0	78.6
Hatta et al./Japan [59]	2017	Multicenter, retrospective cohort	NCR, except for the positive horizontal margin	1,066	8.4	-
Han et al./Korea [60]	2016	Single-center, retrospective cohort	NCR	45	6.7	37.8
Nakata et al./Japan [61]	2016	Single-center, retrospective cohort	NCR	6	0	0
Toyokawa et al./Japan [62]	2016	Multicenter, retrospective cohort	NCR	100	9.0	9.0
Yajima et al./Japan [63]	2015	Single-center, retrospective cohort	NCR	16	0	46.0
Kim et al./Korea [64]	2015	Single-center, retrospective cohort	NCR, except for the positive horizontal margin in differentiated-type	194	5.7	5.2
Yang et al./Korea [65]	2015	Single-center, retrospective cohort	NCR	123	12.2	-
Ito et al./Japan [66]	2013	Single-center, retrospective cohort	NCR	41	9.8	14.6
Abe et al./Japan [67]	2013	Single-center, retrospective cohort	NCR in undifferentiated-type	21	9.5	4.8
Arigami et al./Japan [68]	2013	Single-center, retrospective cohort	NCR	16	12.5	-
Tsujimoto et al./Japan [69]	2012	Single-center, retrospective cohort	Positive horizontal or vertical margin	27	-	40.7
Lee et al./Korea [70]	2011	Single-center, retrospective cohort	Positive horizontal or vertical margin	13	23.1	15.4
Lee et al./Korea [71]	2010	Single-center, retrospective cohort	NCR	28	3.8	28.6
Goto et al./Japan [72]	2008	Single-center, retrospective cohort	NCR	31	12.9	6.5
Ryu et al./Korea [73]	2007	Single-center, retrospective cohort	NCR	43	9.3	39.5
Chung et al./Korea [74]	2007	Single-center, retrospective cohort	Positive horizontal or vertical margin	19	0	44.4
Korenaga et al./Japan [75]	1997	Single-center, retrospective cohort	NCR	11	9.1	36.4

LNM = lymph node metastasis; NCR = non-curative resection; ESD = endoscopic submucosal dissection.

with minimal excision, such as without lymph node dissection, may be necessary, as opposed to simple follow-up. Although additional endoscopic resection is ideal, technical challenges may arise due to fibrosis or swelling at the previous treatment site, or the location of the lesion may limit additional resection. In such cases, ablation therapy with argon plasma coagulation is often employed. An analysis of 76 patients with positive lateral margins who underwent non-curative resection showed that additional endoscopic treatment was

https://doi.org/10.5230/jgc.2025.25.e5

jgc Journal of Gastric Cancer

Table 2. Long-term outcome after additional treatment compared with observation groups in non-curative ESD for EGC

Author/Country	Year	Study design	Study population	No. of case (Gastrectomy/ Observation)	Outcome	Key results
Lee et al./Korea [25]	2024	Single-center, retrospective comparative study	Positive horizontal margin	13/108	OS	No significant difference in OS between groups
Lee et al./Korea [21]	2023	Single-center, retrospective comparative study	NCR	191/152	OS, DFS	Higher OS rate in patients with additional surgery in the eCura high-risk group (95.2% vs. 71.4%)
Makimoto et al./Japan [41]	2022	Single-center, retrospective comparative study	NCR	100/51	OS, DSS	Higher OS rate in patients with additional surgery (87.4% and 73.8%) No significant difference in DSS between groups
Cao et al./China [78]	2022	Multicenter, retrospective comparative study	NCR ≥60 yr of age	36/121	OS, DSS	No significant difference in OS and DSS between groups
Kim et al./Korea [79]	2022	Multicenter, retrospective comparative study, PSM	NCR in undifferentiated-type	133/252	OS, DFS	Higher DFS rate in patients with additional surgery
Iwai et al./Japan [80]	2021	Single-center, retrospective comparative study	NCR, except for the positive horizontal margin	49/46	OS, DSS	High-risk comorbidity (CCI ≥3) is the primary prognostic parameter after NCR
Yang et al./Korea [44]	2021	Multicenter, retrospective comparative study	Positive horizontal margin in undifferentiated-type	40/46	OS	No significant difference in OS between groups
Esaki et al./Japan [81]	2019	Multicenter, retrospective comparative study	NCR, except for the positive horizontal margin	1,064/905	OS, DSS	No significant difference in OS between groups only in patients ≥80 yr
Kim et al./Korea [48]	2019	Single-center, retrospective comparative study	NCR	113/175	OS, DSS, DFS	No significant difference in OS and DSS between groups Higher DFS rate in patients with additional surgery (97.9% vs. 73.5%)
Jeon et al./Korea [82]	2018	Single-center, retrospective comparative study	NCR in undifferentiated-type	18/16	OS, DSS, DFS	No significant difference in OS and DSS between groups Higher DFS rate in patients with additional surgery (100% vs. 84.6%)
Jeon et al./Korea [19]	2018	Single-center, retrospective comparative study	NCR	264/198	DSS, DFS	Higher DSS and DFS rates in patients with additional treatment (96.7% vs. 86.2%, 92.5% vs. 63.0%, respectively)
Yano et al./Japan [50]	2018	Single-center, retrospective comparative study	NCR	118/113	OS, DSS	Higher DSS and OS rates in patients with additional treatment (100% vs. 92.6%, 96.0% vs. 73.3%, respectively)
Hatta et al./Japan [83]	2018	Multicenter, retrospective comparative study	NCR	1,064/905	OS, DFS	Higher cancer-specific mortality in patients with no additional treatment in the high-risk category
Suzuki et al./Japan [53]	2017	Single-center, retrospective comparative study	NCR, except for the positive horizontal margin	356/212	DSS	No significant difference in DSS between groups
Toya et al./Japan [52]	2017	Single-center, retrospective comparative study	NCR with R0 resection	45/21	OS, DSS	Higher OS rate in patients with additional treatment (93.3% vs 76.2%) No significant difference in DSS between groups
Kawata et al./Japan [84]	2017	Single-center, retrospective comparative study	NCR, except for the positive horizontal margin	323/183	OS, DSS	Higher DSS in patients with additional surgery in the lymphovascular invasion group (98.2% vs. 79.1%)
Sumiyoshi et al./Japan [85]	2017	Single-center, retrospective comparative study	NCR ≥75 yr of age	15/17	OS	No significant difference in OS between groups
Eom et al. /Korea [76]	2017	Single-center, retrospective comparative study, PSM	NCR	126/67	OS, DSS	Lower overall mortality in patients with additional surgery (14.5% vs. 26.0%)

(continued to the next page)

https://doi.org/10.5230/jgc.2025.25.e5

jgc Journal of Gastric Cancer

Table 2. (Continued) Long-term outcome after additional treatment compared with observation groups in non-curative ESD for EGC

Author/Country	Year	Study design	Study population	No. of case (Gastrectomy/ Observation)	Outcome	Key results
Suzuki et al./Japan [77]	2017	Multicenter, retrospective comparative study, PSM	NCR, except for the positive horizontal margin	553/553	OS, DSS	Higher OS and DSS in patients with additional surgery (91.0% vs 75.5%, 99.0% vs 96.8%, respectively)
Pyo et al./Korea [86]	2017	Single-center, retrospective comparative study	NCR ≥70 yr of age	87/51	OS, DSS, DFS	A trend toward significance for DSS in favor of the surgery group compared with the surveillance-only group
Jung et al./Korea [87]	2017	Multicenter, retrospective comparative study	NCR ≥75 yr of age	37*/82	OS, DFS	Higher OS rate in patients with additional treatment (86.0% vs. 69.0%)
Hoteya et al./Japan [20]	2016	Single-center, retrospective comparative study	NCR	109/56	OS	No significant difference in OS between groups
Yamanouchi et al./Japan [88]	2016	Single-center, retrospective comparative study	NCR	28/51	OS, DSS	Higher OS rate in patients with additional surgery (91.7% vs. 75.3%)
						No significant difference in DSS between groups
Kim et al./Korea [64]	2015	Single-center, retrospective comparative study	NCR, except for the positive horizontal margin	194/80	OS	Higher OS rate in patients with additional surgery (94.3% vs. 85.0%)
Choi et al./Korea [18]	2015	Multicenter, retrospective comparative study	NCR	28/61	OS, DFS	No significant difference in OS and DFS between groups
Noh et al./Korea [89]	2015	Single-center, retrospective comparative study	Lymphovascular invasion or Positive vertical margins	45/38	DFS	Longer DFS period in patients with additional surgery (78.3±3.4 mo vs. 64.5±4.6 mo)
Yang et al./Korea [65]	2015	Single-center, retrospective comparative study	NCR	123/144	DFS	No significant difference in OS between groups
Abe et al./Japan [90]	2012	Multicenter, retrospective comparative study	NCR, except for the positive horizontal margin, ≥80 yr of age	12/91	OS	No significant difference in OS between the groups
Kusano et al./Japan [91]	2011	Single-center, retrospective comparative study	NCR ≥75 yr of age	38/82	OS, DFS	Higher OS rate in patients with additional surgery (92.0% vs. 63.0%)

ESD = endoscopic submucosal dissection; EGC = early gastric cancer; OS = overall survival; NCR = non-curative resection; DFS = disease-free survival; DSS = disease-specific survival; CCI = Charlson Comorbidity Index; PSM = propensity score matching.
*Includes additional endoscopic treatments.

sufficient regardless of absolute or expanded indications; however, 70.6% had residual cancer. This suggests that endoscopic resection is more appropriate than ablation therapy [58]. Similarly, another study comparing the long-term outcomes of patients with positive lateral margins who underwent repeated ESD, argon plasma coagulation, or surgery found that both endoscopic treatment groups had low local recurrence rates with no reported cancer-related mortality. Based on these results, the authors reported that favorable outcomes could be achieved with endoscopic treatment instead of gastrectomy [42]. A meta-analysis of 7 retrospective studies showed that the recurrence rate was significantly lower with re-endoscopic treatment for positive horizontal resection margins compared to close observation (relative risk, 0.22; 95% confidence interval, 0.06–0.86) but higher compared to gastrectomy (relative risk, 6.45; 95% confidence interval, 1.17–35.52). However, all recurrences were managed with additional endoscopic treatment or surgery [2].

https://doi.org/10.5230/jgc.2025.25.e5

jgc Journal of Gastric Cancer

TREATMENT PLAN AFTER NON-CURATIVE ESD THAT CONSIDERS PATIENT FACTORS

After non-curative resection is confirmed after ESD, pathological curability is a key factor in determining subsequent treatment; however, patient-related factors cannot be neglected. In particular, comorbidities or patient age must be considered in treatment decision-making to weigh the benefits and risks of additional surgery.

In an analysis of patients who were followed up without further treatment after confirmation of non-curative resection following ESD, factors associated with short-term survival of 3 years or less were evaluated. Severe comorbidity, defined as a Charlson Comorbidity Index (CCI) ≥3, was a key factor, with no gastric cancer-related deaths observed. Based on these findings, treatment without additional gastrectomy has been proposed for patients with severe comorbidities [94]. Similar results were found in another retrospective study, in which high-risk comorbidity with a CCI of ≥3 was a clear predictor of unfavorable overall survival, regardless of the additional treatment status in non-curative ESD [80]. Although comorbidities cannot be clearly addressed in the guidelines, they can serve as an important consideration when deciding whether to strictly adhere to the pathological criteria for gastrectomy following non-curative ESD [95]. Other factors, such as nutritional status based on the prognostic nutritional index or the presence of sarcopenia, have also been reported as predictors of unfavorable overall survival after ESD. Patients with these factors often have a poor prognosis, regardless of whether additional treatment is administered following non-curative ESD. Therefore, some argue that the current curability criteria should be expanded to accommodate these patient populations [96-99].

The rate of ESD in the older adult population is increasing, and ESD is recommended, as it is both safe and effective in terms of long-term oncologic outcomes for EGC [100-102]. However, deciding on the treatment approach for older adult patients after non-curative resection is challenging. Current evidence does not provide sufficient information on the maximum age for considering additional gastrectomy and the extent of comorbidities that influence the decision to opt for strict follow-up instead of gastrectomy. Discussions regarding the age threshold at which observation might be preferable to gastrectomy following non-curative ESD are currently ongoing. In general, patient age did not appear to be a greater limiting factor than comorbidities when gastrectomy was considered. On the other hand, however, it has been reported that non-cancer-specific death after gastrectomy is not negligible in very elderly stage I gastric cancer patients aged ≥85 years.[103] A cohort study of patients aged ≥75 years comparing non-curative endoscopic resection with and without surgery found significantly higher overall survival rates (95% vs. 63%) and lower rates of death from gastric cancer recurrence (0% vs. 6.8%) in the surgery group, suggesting that aggressive rescue surgery may still be necessary for older adult patients [91]. Similarly, the 5-year disease-specific survival was 100% in the surgery group compared to 73% in the surveillance group among patients aged ≥70 years with non-curatively endoscopically resected EGC, indicating that gastrectomy should be actively pursued after non-curative resection, even in older adults [86]. However, these studies did not stratify the non-curative resection group according to risk. Therefore, these findings cannot be directly applied in clinical practice. To address this issue, a multicenter analysis using the e-Cura system was conducted in patients aged ≥85 years who underwent non-curative ESD. The study reported that forgoing additional treatment was acceptable in the low- and intermediate-risk groups, whereas additional gastrectomy improved overall survival in the high-risk group among the

https://doi.org/10.5230/jgc.2025.25.e5

oldest-old patients, suggesting that gastrectomy should be considered [104]. In a recent prospective study in Japan, patients aged ≥75 years with LNM risk were further divided into high and low groups based on a 10% estimated metastatic risk within the e-CuraC-2 group. The results indicated that the curability criteria could be expanded to cases where the tumor size was <3 cm and to patients in the elderly-low group [105].

DERIVE NEW TREATMENT ALGORITHMS BEYOND PATHOLOGIC CURABILITY CRITERIA

The current treatment algorithms in the guidelines are straightforward and well-defined, as they were established based on extensive data on LNM risk from various studies. However, in clinical practice, decisions often need to consider patient factors in addition to curability criteria. Although several studies have explored these factors, the evidence remains insufficient to draw definitive conclusions. Nevertheless, it is possible to begin applying new treatment algorithms based on available data, with the understanding that they will need to be refined as higher-quality evidence becomes available. **Fig. 5** illustrates the current treatment algorithms following non-curative ESD recommended by evidence-based guidelines [2,3] and algorithms that could be proposed considering the age and comorbidities of patients.

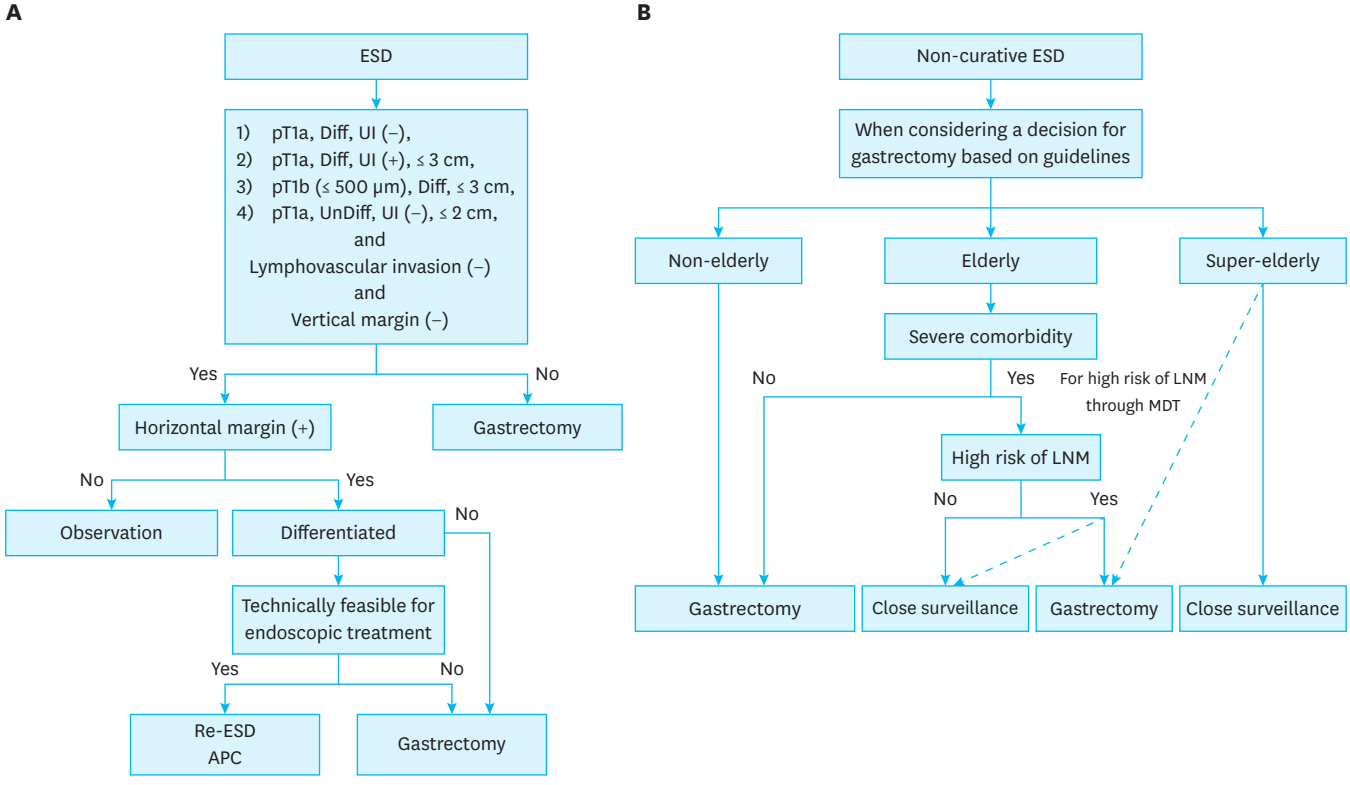

Fig. 5. Guideline-based treatment strategy for early gastric cancer following non-curative ESD (A, adapted from 'Korean Practice Guidelines for Gastric Cancer' [2,3]) and proposed a treatment algorithm incorporating patient factors (B). In this algorithm, age ≥85 years was considered super-elderly, and ≥75 years was considered elderly. In addition, the high-risk group for LNM refers to patients with deep submucosal or lymphovascular invasion.
ESD = endoscopic submucosal dissection; Diff = well or moderately differentiated; UI = ulcer lesion; UnDiff = poorly differentiated/poorly cohesive (including signet ring cells); APC = argon plasma coagulation; MDT = multidisciplinary team; LNM = lymph node metastasis.

https://doi.org/10.5230/jgc.2025.25.e5

jgc Journal of Gastric Cancer

CONCLUSION

In cases of non-curative endoscopic resection for EGC, additional treatment should be based on LNM risk to maximize curability. For patients with high-risk pathological factors, such as lymphatic invasion or deep submucosal invasion, additional gastrectomy is a clear choice. However, in cases with positive horizontal margins, the negligible risk of LNM makes endoscopic treatment a reasonable option. Indeed, repeat endoscopic resection is more appropriate than argon plasma coagulation therapy for ensuring complete resection. Most importantly, patient factors, such as age and comorbidities, must be considered in addition to pathological curability when planning further treatment. Other factors, including sarcopenia and nutritional status, have also been shown to affect treatment decisions. Treatment strategies should aim to minimize not only GC-specific mortality but also all-cause mortality in consideration of these additional factors.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209-249. PUBMED | CROSSREF
2. Kim TH, Kim IH, Kang SJ, Choi M, Kim BH, Eom BW, et al. Korean practice guidelines for gastric cancer 2022: an evidence-based, multidisciplinary approach. J Gastric Cancer 2023;23:3-106. PUBMED | CROSSREF
3. Kim IH, Kang SJ, Choi W, Seo AN, Eom BW, Kang B, et al. Korean practice guidelines for gastric cancer 2024: an evidence-based, multidisciplinary approach (update of 2022 guideline). J Gastric Cancer 2025;25:5-114. CROSSREF
4. Collatuzzo G, Santucci C, Malvezzi M, La Vecchia C, Boffetta P, Negri E. Trends in gastric cancer mortality 1990-2019 in 36 countries worldwide, with predictions to 2025, and incidence, overall and by subtype. Cancer Med 2023;12:9912-9925. PUBMED | CROSSREF
5. Pyo JH, Lee H, Min BH, Lee JH, Choi MG, Lee JH, et al. 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. PUBMED | CROSSREF
6. Lee H, Yun WK, Min BH, Lee JH, Rhee PL, Kim KM, et al. A feasibility study on the expanded indication for endoscopic submucosal dissection of early gastric cancer. Surg Endosc 2011;25:1985-1993. PUBMED | CROSSREF
7. Park CH, Shin S, Park JC, Shin SK, Lee SK, Lee YC, et al. Long-term outcome of early gastric cancer after endoscopic submucosal dissection: expanded indication is comparable to absolute indication. Dig Liver Dis 2013;45:651-656. PUBMED | CROSSREF
8. Park SW, Lee H, Park CH, Jang HJ, Ahn H. Endoscopic and oncologic outcomes according to indication criteria of endoscopic resection for early gastric cancer: a systematic review and meta-analysis. Surg Endosc 2016;30:1270-1281. PUBMED | CROSSREF
9. Kim SG. Endoscopic treatment for early gastric cancer. J Gastric Cancer 2011;11:146-154. PUBMED | CROSSREF
10. Hatta W, Gotoda T, Koike T, Uno K, Asano N, Imatani A, et al. Is additional gastrectomy required for elderly patients after endoscopic submucosal dissection with endoscopic curability C-2 for early gastric cancer? Digestion 2022;103:83-91. PUBMED | CROSSREF
11. Na JE, Kim YG, Kim TJ, Lee H, Min YW, Min BH, et al. Long-term safety of delayed surgery after upfront endoscopic resection for early gastric cancer: a propensity matched study. Ann Surg Oncol 2021;28:106-113. PUBMED | CROSSREF
12. Park CH, Yang DH, Kim JW, Kim JH, Kim JH, Min YW, et al. Clinical practice guideline for endoscopic resection of early gastrointestinal cancer. Clin Endosc 2020;53:142-166. PUBMED | CROSSREF
13. Hatta W, Gotoda T, Oyama T, Kawata N, Takahashi A, Yoshifuku Y, et al. A scoring system to stratify curability after endoscopic submucosal dissection for early gastric cancer: "eCura system". Am J Gastroenterol 2017;112:874-881. PUBMED | CROSSREF
14. Ono H, Yao K, Fujishiro M, Oda I, Uedo N, Nimura S, et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer (second edition). Dig Endosc 2021;33:4-20. PUBMED | CROSSREF

https://doi.org/10.5230/jgc.2025.25.e5

15. 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. PUBMED | CROSSREF
16. Suzuki H, Ono H, Hirasawa T, Takeuchi Y, Ishido K, Hoteya S, et al. Long-term survival after endoscopic resection for gastric cancer: real-world evidence from a multicenter prospective cohort. Clin Gastroenterol Hepatol 2023;21:307-318.e2. PUBMED | CROSSREF
17. Ahn JY, Jung HY, Choi JY, Kim MY, Lee JH, Choi KS, et al. Natural course of noncurative endoscopic resection of differentiated early gastric cancer. Endoscopy 2012;44:1114-1120. PUBMED | CROSSREF
18. Choi JY, Jeon SW, Cho KB, Park KS, Kim ES, Park CK, et al. Non-curative endoscopic resection does not always lead to grave outcomes in submucosal invasive early gastric cancer. Surg Endosc 2015;29:1842-1849. PUBMED | CROSSREF
19. Jeon MY, Park JC, Hahn KY, Shin SK, Lee SK, Lee YC. Long-term outcomes after noncurative endoscopic resection of early gastric cancer: the optimal time for additional endoscopic treatment. Gastrointest Endosc 2018;87:1003-1013.e2. PUBMED | CROSSREF
20. Hoteya S, Iizuka T, Kikuchi D, Ogawa O, Mitani T, Matsui A, et al. Clinicopathological outcomes of patients with early gastric cancer after non-curative endoscopic submucosal dissection. Digestion 2016;93:53-58. PUBMED | CROSSREF
21. Lee S, Kim SG, Cho SJ. Decision to perform additional surgery after non-curative endoscopic submucosal dissection for gastric cancer based on the risk of lymph node metastasis: a long-term follow-up study. Surg Endosc 2023;37:7738-7748. PUBMED | CROSSREF
22. Yamada S, Hatta W, Shimosegawa T, Takizawa K, Oyama T, Kawata N, et al. Different risk factors between early and late cancer recurrences in patients without additional surgery after noncurative endoscopic submucosal dissection for early gastric cancer. Gastrointest Endosc 2019;89:950-960. PUBMED | CROSSREF
23. Sekiguchi M, Suzuki H, Oda I, Abe S, Nonaka S, Yoshinaga S, et al. Risk of recurrent gastric cancer after endoscopic resection with a positive lateral margin. Endoscopy 2014;46:273-278. PUBMED | CROSSREF
24. Numata N, Oka S, Tanaka S, Kagemoto K, Sanomura Y, Yoshida S, et al. Risk factors and management of positive horizontal margin in early gastric cancer resected by en bloc endoscopic submucosal dissection. Gastric Cancer 2015;18:332-338. PUBMED | CROSSREF
25. Lee JH, Kim SG, Cho SJ. Long-term outcomes of patients with early gastric cancer who had lateral resection margin-positive tumors based on pathology following endoscopic submucosal dissection. J Gastric Cancer 2024;24:199-209. PUBMED | CROSSREF
26. Yoon H, Kim SG, Choi J, Im JP, Kim JS, Kim WH, et al. Risk factors of residual or recurrent tumor in patients with a tumor-positive resection margin after endoscopic resection of early gastric cancer. Surg Endosc 2013;27:1561-1568. PUBMED | CROSSREF
27. Oh YJ, Kim DH, Han WH, Eom BW, Kim YI, Yoon HM, et al. Risk factors for lymph node metastasis in early gastric cancer without lymphatic invasion after endoscopic submucosal dissection. Eur J Surg Oncol 2021;47:3059-3063. PUBMED | CROSSREF
28. Pyo JH, Shin CM, Lee H, Min BH, Lee JH, Kim SM, et al. A risk-prediction model based on lymph-node metastasis for incorporation into a treatment algorithm for signet ring cell-type intramucosal gastric cancer. Ann Surg 2016;264:1038-1043. PUBMED | CROSSREF
29. Pyo JH, Lee H, Min BH, Lee JH, Choi MG, Lee JH, et al. A risk prediction model based on lymph-node metastasis in poorly differentiated-type intramucosal gastric cancer. PLoS One 2016;11:e0156207. PUBMED | CROSSREF
30. Yang P, Zheng XD, Wang JM, Geng WB, Wang X. Undifferentiated-predominant mixed-type early gastric cancer is more aggressive than pure undifferentiated type: a systematic review and meta-analysis. BMJ Open 2022;12:e054473. PUBMED | CROSSREF
31. Hirai Y, Abe S, Makiguchi ME, Sekiguchi M, Nonaka S, Suzuki H, et al. Endoscopic resection of undifferentiated early gastric cancer. J Gastric Cancer 2023;23:146-158. PUBMED | CROSSREF
32. Pyo JH, Ahn S, Lee H, Min BH, Lee JH, Shim SG, et al. Clinicopathological features and prognosis of mixed-type T1a gastric cancer based on Lauren's classification. Ann Surg Oncol 2016;23:784-791. PUBMED | CROSSREF
33. Pyo JH, Lee H, Min BH, Lee JH, Choi MG, Lee JH, et al. Early gastric cancer with a mixed-type Lauren classification is more aggressive and exhibits greater lymph node metastasis. J Gastroenterol 2017;52:594-601. PUBMED | CROSSREF
34. Takeuchi H, Abe N, Hashimoto Y, Ooki A, Nagao G, Hirano K, et al. Establishment of pathological quantitative method for determining undifferentiated component ratio in patients with differentiated/undifferentiated mixed-type early gastric cancer and clinical significance of this ratio. Gastric Cancer 2018;21:661-671. PUBMED | CROSSREF

35. Yang HJ, Kim YI, Ahn JY, Choi KD, Kim SG, Jeon SW, et al. External validation of the eCura system for undifferentiated-type early gastric cancer with noncurative endoscopic resection. Gut Liver 2023;17:537-546. PUBMED | CROSSREF
36. Yang HJ, Lee H, Kim TJ, Jung DH, Choi KD, Ahn JY, et al. A modified eCura system to stratify the risk of lymph node metastasis in undifferentiated-type early gastric cancer after endoscopic resection. J Gastric Cancer 2024;24:172-184. PUBMED | CROSSREF
37. Morais R, Libanio D, Dinis Ribeiro M, Ferreira A, Barreiro P, Bourke MJ, et al. Predicting residual neoplasia after a non-curative gastric ESD: validation and modification of the eCura system in the Western setting: the W-eCura score. Gut 2024;73:105-117. PUBMED | CROSSREF
38. Jin CQ, Zhao J, Ding XY, Yu LL, Ye GL, Zhu XJ, et al. Clinical outcomes and risk factors of non-curative endoscopic submucosal dissection for early gastric cancer: a retrospective multicenter study in Zhejiang, China. Front Oncol 2023;13:1225702. PUBMED | CROSSREF
39. Sun F, Huang Y, Sun Y, Wang X, Ai S, Guan W, et al. Risk factors of additional surgery after non-curative endoscopic submucosal dissection for early gastric cancer. BMC Gastroenterol 2023;23:383. PUBMED | CROSSREF
40. Park SH, Yoon HM, Ryu KW, Kim YW, Kook MC, Eom BW. Risks and benefits of additional surgery for early gastric cancer in the upper third of the stomach meeting non-curative resection criteria after endoscopic submucosal dissection. World J Surg Oncol 2022;20:311. PUBMED | CROSSREF
41. Makimoto S, Mushiake Y, Takami T, Shintani H, Kataoka N, Yamaguchi T, et al. Evaluation of additional gastrectomy after noncurative endoscopic submucosal dissection for early gastric cancer. BMC Surg 2022;22:352. PUBMED | CROSSREF
42. Kim TS, Min BH, Min YW, Lee H, Rhee PL, Kim JJ, et al. Long-term outcomes of additional endoscopic treatments for patients with positive lateral margins after endoscopic submucosal dissection for early gastric cancer. Gut Liver 2022;16:547-554. PUBMED | CROSSREF
43. Yang HJ, Jang JY, Kim SG, Ahn JY, Nam SY, Kim JH, et al. Risk factors of lymph node metastasis after non-curative endoscopic resection of undifferentiated-type early gastric cancer. Gastric Cancer 2021;24:168-178. PUBMED | CROSSREF
44. Yang HJ, Lee WS, Lee BE, Ahn JY, Jang JY, Lim JH, et al. Long-term outcomes of undifferentiated-type early gastric cancer with positive horizontal margins after endoscopic resection. Gut Liver 2021;15:723-731. PUBMED | CROSSREF
45. Jeong U, Bang HY, Kim PS. Clinical significance of additional gastrectomy after non-curative endoscopic submucosal dissection for early gastric cancer: a retrospective single-center study. Korean J Clin Oncol 2021;17:68-72. PUBMED | CROSSREF
46. Kang HJ, Chung H, Kim SG, Kim J, Kim JL, Lee E, et al. Synergistic effect of lymphatic invasion and venous invasion on the risk of lymph node metastasis in patients with non-curative endoscopic resection of early gastric cancer. J Gastrointest Surg 2020;24:1499-1509. PUBMED | CROSSREF
47. Tian YT, Ma FH, Wang GQ, Zhang YM, Dou LZ, Xie YB, et al. Additional laparoscopic gastrectomy after noncurative endoscopic submucosal dissection for early gastric cancer: a single-center experience. World J Gastroenterol 2019;25:3996-4006. PUBMED | CROSSREF
48. Kim HJ, Kim SG, Kim J, Hong H, Lee HJ, Kim MS, et al. Clinical outcomes of early gastric cancer with non-curative resection after pathological evaluation based on the expanded criteria. PLoS One 2019;14:e0224614. PUBMED | CROSSREF
49. Suzuki H, Takizawa K, Hirasawa T, Takeuchi Y, Ishido K, Hoteya S, et al. Short-term outcomes of multicenter prospective cohort study of gastric endoscopic resection: 'real-world evidence' in Japan. Dig Endosc 2019;31:30-39. PUBMED | CROSSREF
50. Yano T, Ishido K, Tanabe S, Wada T, Azuma M, Kawanishi N, et al. 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. PUBMED | CROSSREF
51. Jung DH, Huh CW, Kim JH, Hong JH, Park JC, Lee YC, et al. Risk-stratification model based on lymph node metastasis after noncurative endoscopic resection for early gastric cancer. Ann Surg Oncol 2017;24:1643-1649. PUBMED | CROSSREF
52. Toya Y, Endo M, Nakamura S, Akasaka R, Kosaka T, Yanai S, et al. Clinical outcomes of non-curative endoscopic submucosal dissection with negative resected margins for gastric cancer. Gastrointest Endosc 2017;85:1218-1224. PUBMED | CROSSREF
53. Suzuki H, Oda I, Abe S, Sekiguchi M, Nonaka S, Yoshinaga S, et al. Clinical outcomes of early gastric cancer patients after noncurative endoscopic submucosal dissection in a large consecutive patient series. Gastric Cancer 2017;20:679-689. PUBMED | CROSSREF

54. Probst A, Schneider A, Schaller T, Anthuber M, Ebigbo A, Messmann H. Endoscopic submucosal dissection for early gastric cancer: are expanded resection criteria safe for Western patients? Endoscopy 2017;49:855-865. PUBMED | CROSSREF
55. Kim HS, Ahn JY, Kim SO, Kim BS. Can further gastrectomy be avoided in patients with incomplete endoscopic resection? Surg Endosc 2017;31:4735-4748. PUBMED | CROSSREF
56. Goto A, Nishikawa J, Hideura E, Ogawa R, Nagao M, Sasaki S, et al. Lymph node metastasis can be determined by just tumor depth and lymphovascular invasion in early gastric cancer patients after endoscopic submucosal dissection. Eur J Gastroenterol Hepatol 2017;29:1346-1350. PUBMED | CROSSREF
57. Sunagawa H, Kinoshita T, Kaito A, Shibasaki H, Kaneko K, Ochiai A, et al. 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. PUBMED | CROSSREF
58. Kim HW, Kim JH, Park JC, Jeon MY, Lee YC, Lee SK, et al. 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. PUBMED | CROSSREF
59. Hatta W, Gotoda T, Oyama T, Kawata N, Takahashi A, Yoshifuku Y, et al. Is radical surgery necessary in all patients who do not meet the curative criteria for endoscopic submucosal dissection in early gastric cancer? A multi-center retrospective study in Japan. J Gastroenterol 2017;52:175-184. PUBMED | CROSSREF
60. Han JP, Hong SJ, Kim HK, Lee YN, Lee TH, Ko BM, et al. Risk stratification and management of non-curative resection after endoscopic submucosal dissection for early gastric cancer. Surg Endosc 2016;30:184-189. PUBMED | CROSSREF
61. Nakata B, Tendo M, Okuyama M, Nakahara K, Ishizu H, Masuda G, et al. Additional surgical resection after endoscopic mucosal dissection for early gastric cancer: a medium-sized hospital's experience. Int J Surg 2016;36:335-341. PUBMED | CROSSREF
62. Toyokawa T, Ohira M, Tanaka H, Minamino H, Sakurai K, Nagami Y, et al. Optimal management for patients not meeting the inclusion criteria after endoscopic submucosal dissection for gastric cancer. Surg Endosc 2016;30:2404-2414. PUBMED | CROSSREF
63. Yajima H, Omura N, Takahashi N, Yoshida K, Yanaga K. Additional gastrectomy after endoscopic mucosal resection for early gastric cancer. Int Surg 2015;100:169-172. PUBMED | CROSSREF
64. Kim ER, Lee H, Min BH, Lee JH, Rhee PL, Kim JJ, et al. Effect of rescue surgery after non-curative endoscopic resection of early gastric cancer. Br J Surg 2015;102:1394-1401. PUBMED | CROSSREF
65. Yang HJ, Kim SG, Lim JH, Choi J, Im JP, Kim JS, et al. Predictors of lymph node metastasis in patients with non-curative endoscopic resection of early gastric cancer. Surg Endosc 2015;29:1145-1155. PUBMED | CROSSREF
66. Ito H, Inoue H, Ikeda H, Odaka N, Yoshida A, Satodate H, et al. Surgical outcomes and clinicopathological characteristics of patients who underwent potentially noncurative endoscopic resection for gastric cancer: a report of a single-center experience. Gastroenterol Res Pract 2013;2013:427405. PUBMED | CROSSREF
67. Abe S, Oda I, Suzuki H, Nonaka S, Yoshinaga S, Odagaki T, et al. Short- and long-term outcomes of endoscopic submucosal dissection for undifferentiated early gastric cancer. Endoscopy 2013;45:703-707. PUBMED | CROSSREF
68. Arigami T, Uenosono Y, Yanagita S, Matsushita D, Arima H, Hirata M, et al. Feasibility of sentinel node navigation surgery after noncurative endoscopic resection for early gastric cancer. J Gastroenterol Hepatol 2013;28:1343-1347. PUBMED | CROSSREF
69. Tsujimoto H, Ogata S, Yaguchi Y, Kumano I, Takahata R, Ono S, et al. Predictive value of the pathological extent of tumor invasion in endoscopic resection margins positive for residual tumor cells in surgically resected specimens of early gastric cancer. Exp Ther Med 2012;4:507-513. PUBMED | CROSSREF
70. Lee HJ, Jang YJ, Kim JH, Park SS, Park SH, Park JJ, et al. Clinical outcomes of gastrectomy after incomplete EMR/ESD. J Gastric Cancer 2011;11:162-166. PUBMED | CROSSREF
71. Lee JH, Kim JH, Kim DH, Jeon TY, Kim DH, Kim GH, et al. Is surgical treatment necessary after non-curative endoscopic resection for early gastric cancer? J Gastric Cancer 2010;10:182-187. PUBMED | CROSSREF
72. Goto O, Fujishiro M, Kakushima N, Kodashima S, Ono S, Yamaguchi H, et al. Endoscopic submucosal dissection as a staging measure may not lead to worse prognosis in early gastric cancer patients with additional gastrectomy. Dig Liver Dis 2008;40:293-297. PUBMED | CROSSREF
73. Ryu KW, Choi IJ, Doh YW, Kook MC, Kim CG, Park HJ, et al. Surgical indication for non-curative endoscopic resection in early gastric cancer. Ann Surg Oncol 2007;14:3428-3434. PUBMED | CROSSREF
74. Chung YS, Park DJ, Lee HJ, Kim SG, Jung HC, Song IS, et al. The role of surgery after incomplete endoscopic mucosal resection for early gastric cancer. Surg Today 2007;37:114-117. PUBMED | CROSSREF

75. Korenaga D, Orita H, Maekawa S, Maruoka A, Sakai K, Ikeda T, et al. Pathological appearance of the stomach after endoscopic mucosal resection for early gastric cancer. Br J Surg 1997;84:1563-1566. PUBMED | CROSSREF
76. Eom BW, Kim YI, Kim KH, Yoon HM, Cho SJ, Lee JY, et al. Survival benefit of additional surgery after noncurative endoscopic resection in patients with early gastric cancer. Gastrointest Endosc 2017;85:155-163.e3. PUBMED | CROSSREF
77. Suzuki S, Gotoda T, Hatta W, Oyama T, Kawata N, Takahashi A, et al. Survival benefit of additional surgery after non-curative endoscopic submucosal dissection for early gastric cancer: a propensity score matching analysis. Ann Surg Oncol 2017;24:3353-3360. PUBMED | CROSSREF
78. Cao W, Liu S, Wang S, Wang S, Song Y, He Y. Effect of charlson comorbidity index and treatment strategy on survival of elderly patients after endoscopic submucosal dissection for gastric adenocarcinoma: a multicenter retrospective study. Front Public Health 2022;9:803113. PUBMED | CROSSREF
79. Kim JH, Kim YI, Ahn JY, Shin WG, Yang HJ, Nam SY, et al. Long-term outcomes of endoscopic resection followed by additional surgery after non-curative resection in undifferentiated-type early gastric cancer: a nationwide multi-center study. Surg Endosc 2022;36:1847-1856. PUBMED | CROSSREF
80. Iwai N, Dohi O, Naito Y, Inada Y, Inoue K, Okayama T, et al. High-risk comorbidity influences prognosis in early gastric cancer after noncurative endoscopic submucosal dissection: a retrospective study. Dig Dis 2021;39:96-105. PUBMED | CROSSREF
81. Esaki M, Hatta W, Shimosegawa T, Oyama T, Kawata N, Takahashi A, et al. Age affects clinical management after noncurative endoscopic submucosal dissection for early gastric cancer. Dig Dis 2019;37:423-433. PUBMED | CROSSREF
82. Jeon HK, Lee SJ, Kim GH, Park DY, Lee BE, Song GA. Endoscopic submucosal dissection for undifferentiated-type early gastric cancer: short- and long-term outcomes. Surg Endosc 2018;32:1963-1970. PUBMED | CROSSREF
83. Hatta W, Gotoda T, Oyama T, Kawata N, Takahashi A, Yoshifuku Y, et al. Is the eCura system useful for selecting patients who require radical surgery after noncurative endoscopic submucosal dissection for early gastric cancer? A comparative study. Gastric Cancer 2018;21:481-489. PUBMED | CROSSREF
84. Kawata N, Kakushima N, Takizawa K, Tanaka M, Makuuchi R, Tokunaga M, et al. Risk factors for lymph node metastasis and long-term outcomes of patients with early gastric cancer after non-curative endoscopic submucosal dissection. Surg Endosc 2017;31:1607-1616. PUBMED | CROSSREF
85. Sumiyoshi T, Kondo H, Fujii R, Minagawa T, Fujie S, Kimura T, et al. Short- and long-term outcomes of endoscopic submucosal dissection for early gastric cancer in elderly patients aged 75 years and older. Gastric Cancer 2017;20:489-495. PUBMED | CROSSREF
86. Pyo JH, Lee H, Min BH, Lee JH, Kim KM, Yoo H, et al. Comparison of long-term outcomes after non-curative endoscopic resection in older patients with early gastric cancer. Ann Surg Oncol 2017;24:2624-2631. PUBMED | CROSSREF
87. Jung DH, Lee YC, Kim JH, Lee SK, Shin SK, Park JC, et al. Additive treatment improves survival in elderly patients after non-curative endoscopic resection for early gastric cancer. Surg Endosc 2017;31:1376-1382. PUBMED | CROSSREF
88. Yamanouchi K, Ogata S, Sakata Y, Tsuruoka N, Shimoda R, Nakayama A, et al. Effect of additional surgery after noncurative endoscopic submucosal dissection for early gastric cancer. Endosc Int Open 2016;4:E24-E29. PUBMED | CROSSREF
89. Noh GY, Ku HR, Kim YJ, Park SC, Kim J, Han CJ, et al. Clinical outcomes of early gastric cancer with lymphovascular invasion or positive vertical resection margin after endoscopic submucosal dissection. Surg Endosc 2015;29:2583-2589. PUBMED | CROSSREF
90. Abe N, Gotoda T, Hirasawa T, Hoteya S, Ishido K, Ida Y, et al. Multicenter study of the long-term outcomes of endoscopic submucosal dissection for early gastric cancer in patients 80 years of age or older. Gastric Cancer 2012;15:70-75. PUBMED | CROSSREF
91. Kusano C, Iwasaki M, Kaltenbach T, Conlin A, Oda I, Gotoda T. Should elderly patients undergo additional surgery after non-curative endoscopic resection for early gastric cancer? Long-term comparative outcomes. Am J Gastroenterol 2011;106:1064-1069. PUBMED | CROSSREF
92. Pimentel-Nunes P, Libânio D, Bastiaansen BAJ, Bhandari P, Bisschops R, Bourke MJ, et al. Endoscopic submucosal dissection for superficial gastrointestinal lesions: European Society of Gastrointestinal Endoscopy (ESGE) guideline - update 2022. Endoscopy 2022;54:591-622. PUBMED | CROSSREF
93. Ishii N, Omata F, Fujisaki J, Hirasawa T, Kaise M, Hoteya S, et al. Management of early gastric cancer with positive horizontal or indeterminable margins after endoscopic submucosal dissection: multicenter survey. Endosc Int Open 2017;5:E354-E362. PUBMED | CROSSREF

94. Shimada T, Yamagata T, Kanno Y, Ohira T, Harada Y, Koike Y, et al. Predictive factors for short-term survival after non-curative endoscopic submucosal dissection for early gastric cancer. Digestion 2021;102:630-639. PUBMED | CROSSREF
95. Toya Y, Endo M, Nakamura S, Akasaka R, Yanai S, Kawasaki K, et al. Long-term outcomes and prognostic factors with non-curative endoscopic submucosal dissection for gastric cancer in elderly patients aged ≥ 75 years. Gastric Cancer 2019;22:838-844. PUBMED | CROSSREF
96. Kim GH, Choi KD, Ko Y, Park T, Kim KW, Park SY, et al. Impact of comorbidities, sarcopenia, and nutritional status on the long-term outcomes after endoscopic submucosal dissection for early gastric cancer in elderly patients aged ≥ 80 years. Cancers (Basel) 2021;13:3598. PUBMED | CROSSREF
97. Iwai N, Dohi O, Naito Y, Inada Y, Fukui A, Takayama S, et al. Impact of the Charlson comorbidity index and prognostic nutritional index on prognosis in patients with early gastric cancer after endoscopic submucosal dissection. Dig Endosc 2018;30:616-623. PUBMED | CROSSREF
98. Hisada H, Tsuji Y, Obata M, Cho R, Nagao S, Miura Y, et al. The impact of sarcopenia on short- and long-term outcomes of endoscopic submucosal dissection for early gastric cancer. J Gastroenterol 2022;57:952-961. PUBMED | CROSSREF
99. Sekiguchi M, Oda I, Suzuki H, Abe S, Nonaka S, Yoshinaga S, et al. Clinical outcomes and prognostic factors in gastric cancer patients aged ≥85 years undergoing endoscopic submucosal dissection. Gastrointest Endosc 2017;85:963-972. PUBMED | CROSSREF
100. Kim TJ, Pyo JH, Lee H, Choi SC, Min YW, Min BH, et al. Outcomes of endoscopic resection for early gastric cancer in very elderly patients: a nationwide population-based study. Gut Liver 2023;17:529-536. PUBMED | CROSSREF
101. Park CH, Lee H, Kim DW, Chung H, Park JC, Shin SK, et al. Clinical safety of endoscopic submucosal dissection compared with surgery in elderly patients with early gastric cancer: a propensity-matched analysis. Gastrointest Endosc 2014;80:599-609. PUBMED | CROSSREF
102. Lee SH, Cho H, Lim MN, Nam SJ. National statistics of endoscopic submucosal dissection for early gastric cancer in Korea. J Gastric Cancer 2024;24:464-478. PUBMED | CROSSREF
103. Konishi H, Ichikawa D, Itoh H, Fukuda K, Kakihara N, Takemura M, et al. Surgery for gastric cancer patients of age 85 and older: multicenter survey. World J Gastroenterol 2017;23:1215-1223. PUBMED | CROSSREF
104. Hatta W, Toya Y, Shimada T, Hamada K, Watanabe K, Nakamura J, et al. Treatment strategy after noncurative endoscopic resection for early gastric cancers in patients aged ≥ 85 years: a multicenter retrospective study in a highly aged area of Japan. J Gastroenterol 2023;58:346-357. PUBMED | CROSSREF
105. Sekiguchi M, Suzuki H, Takizawa K, Hirasawa T, Takeuchi Y, Ishido K, et al. Potential for expanding indications and curability criteria of endoscopic resection for early gastric cancer in elderly patients: results from a Japanese multicenter prospective cohort study. Gastrointest Endosc 2024;100:438-448.e1. PUBMED | CROSSREF