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CLINICAL ENDOSCOPY

Outcomes of endoscopic submucosal dissection for superficial esophageal neoplasms in patients with liver cirrhosis

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Background/Aims: The treatment of superficial esophageal neoplasms (SENs) in cirrhotic patients is challenging and rarely investigated. We evaluated the outcomes of endoscopic submucosal dissection (ESD) to determine the efficacy and safety of treating SENs in patients with liver cirrhosis.

Methods: The baseline characteristics and treatment outcomes of patients who underwent ESD for SENs between November 2005 and December 2017 were retrospectively reviewed.

Results: ESD was performed in 437 patients with 481 SENs, including 15 cirrhotic patients with 17 SENs. *En bloc* resection (88.2% vs. 97.0%) and curative resection (64.7% vs. 78.9%) rates were not different between the cirrhosis and non-cirrhosis groups (p=0.105 and p=0.224, respectively). Bleeding was more common in cirrhotic patients (p=0.054), and all cases were successfully controlled endoscopically. The median procedure and hospitalization duration did not differ between the groups. Overall survival was lower in cirrhotic patients (p=0.003), while disease-specific survival did not differ between the groups (p=0.85).

Conclusions: ESD could be a safe and effective treatment option for SENs in patients with cirrhosis. Detailed preprocedural assessments are needed, including determination of liver function, esophageal varix status, and remaining life expectancy, to identify patients who will obtain the greatest benefit.

Keywords: Endoscopic mucosal resection; Esophageal neoplasms; Liver cirrhosis; Squamous cell carcinoma

INTRODUCTION

The implementation of nationwide endoscopic screening programs and the development of new endoscopic imaging techniques, such as narrow-band imaging, have made early detection of superficial esophageal neoplasms (SENs) possible.[1] Although open or minimally invasive esophagectomy is accepted as the treatment of choice for esophageal cancer,[2] there remains concern because esophagectomy is associated with high rates of mortality and morbidity.[3] Therefore, endoscopic submucosal dissection (ESD) is now accepted as one of the possible treatment options for SENs with a low risk of lymph node metastasis because it has shown potential efficacy and safety at a high rate of complete resection and low rate of adverse events.[4]

Patients with liver cirrhosis have a high possibility of esophageal neoplasms because alcohol consumption is a risk factor for esophageal cancer and liver cirrhosis.[5] In a previous study, 7%

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of patients who underwent esophagectomy had pathologically proven liver cirrhosis.[6] Deciding to perform esophagectomy in patients with cirrhosis is particularly difficult, as dismal outcomes of 50% in-hospital mortality in Child-Pugh class B and 100% in class C patients with cirrhosis have been reported in a previous study.[7] Therefore, if its use is feasible, ESD could be a more desirable option in patients with cirrhosis as it is a much less invasive procedure than esophagectomy.

However, esophageal ESD is considered more difficult to perform in patients with cirrhosis than in the general population, as cirrhotic patients usually have a higher tendency to bleed and sometimes have esophageal varices that could hinder the ESD procedure. However, to the best of our knowledge, this topic has not been adequately investigated. Only two studies have evaluated the short-term outcomes of ESD for SENs in patients with liver cirrhosis.[8,9] As these two studies included a small sample (<10 patients), it remains unclear whether esophageal ESD is safe to perform in patients with cirrhosis.

In this study, we report the clinical outcomes of esophageal ESD in cirrhotic patients and compare the results with those in non-cirrhotic patients. Furthermore, we evaluated the change in Child-Pugh classification status before and after esophageal ESD in cirrhotic patients to determine the safety of the procedure in terms of liver function.

METHODS

Patients

Patients who underwent ESD for SENs at a tertiary university hospital between April 2005 and December 2017 were considered eligible for this study. Patients who underwent endoscopic mucosal resection were excluded from the study. The medical records of the patients were retrospectively reviewed, and data on the clinical characteristics of the patients, tumor characteristics, and procedural factors were investigated. Furthermore, data on the clinical outcomes of endoscopic resection, recurrence rates, and disease-specific and overall survival rates were analyzed.

A review of medical records identified 17 SENs in 15 patients with cirrhosis, among all included patients. The shape and location of the esophageal varices were evaluated according to the general rules for recording endoscopic findings of esophagogastric varices.[10] Child-Pugh classification was used to assess liver function in patients with cirrhosis. To evaluate the efficacy and safety of esophageal ESD in patients with cirrhosis, the clinical data of these patients were compared with those of 422 non-cirrhotic control patients with 464 SENs.

Procedures and follow-up

Endoscopic examination with white-light imaging, Lugol chromoendoscopy, and narrow-band imaging was performed to confirm the exact margin of the tumor before ESD. Endoscopic ultrasonography and computed tomography (CT) were performed to evaluate the depth of tumor invasion and lymph node status. Positron emission tomography was performed in patients with invasive carcinoma to detect possible distant metastases. With patients under conscious sedation or general anesthesia, ESD procedures were performed by highly experienced endoscopists in a standardized manner, as described previously.[11]

Blood tests for complete blood cell count were performed the day after the procedure, and chest radiography was performed to identify the presence of pneumomediastinum or capnomediastinum. Second-look endoscopy was generally not performed unless requested by the practicing endoscopist, due to the perceived high risk of bleeding. Proton pump inhibitors were administered intravenously from the morning of the procedure to the end of the non-per-os period. Follow-up endoscopic examination was performed every 6 months for the first 2 years after ESD and every year thereafter. Chest CT was performed biannually for the first 2 years after ESD and annually until 5 years in patients with invasive carcinoma. Positron emission tomography and CT were performed at 1, 3, and 5 years after endoscopic resection.

Histopathological evaluation

Histopathological evaluation was performed as described previously.[11] Resected specimens were fixed with formalin and sliced at 2-mm intervals. The specimens were pathologically reviewed according to the guidelines of the Clinical and Pathological Studies in Carcinoma of the Esophagus.[12,13]

The depth of invasion was classified into five categories: T0, dysplasia; M1, carcinoma *in situ*; M2, tumor invading the lamina propria; M3, tumor involving the muscularis mucosa; and submucosal invasion, defined as a tumor invading beyond the muscularis mucosa, including SM1 (tumor invasion <200 μm from the muscularis mucosa) and SM2 (tumor invasion >200 μm from the muscularis mucosa).[14]

Definitions

En bloc resection was defined as a single-piece resection without fragmentation, regardless of the depth of invasion and lympho-

vascular invasion. Complete resection was defined as tumor-free lateral and vertical margins on histological examination. Tumors removed in piecemeal resection were considered completely resected when evaluating the margins after achieving a perfect reconstruction of all pieces was possible. Curative resection was defined as the absence of a poorly differentiated feature, lymphovascular involvement, or submucosal invasion in the *en bloc* resected specimen. Tumors that did not meet the abovementioned criteria were considered non-curatively resected despite complete resection.

Synchronous lesions were defined as tumors detected at a different location within 1 year of initial endoscopic resection, and metachronous lesions were those detected >1 year after endoscopic resection.

Bleeding was defined as a condition that requires endoscopic hemostasis and the presence of clinical symptoms such as hematemesis or melena. Perforation was considered to have occurred when mediastinal connective tissue was visible during the procedure or radiographically as the presence of free air on chest radiography. The stricture was defined as the presence of a standard endoscope (GIF-H260; Olympus, Tokyo, Japan) with a front-end diameter of 9.8 mm that could not pass through the ESD site.

Liver cirrhosis was diagnosed based on imaging findings, including abdominal ultrasonography and CT, laboratory findings, and medical history indicating portal hypertension, such as the presence of esophageal varices.

Statistical analysis

Differences between the cirrhosis and non-cirrhosis groups were analyzed using Fisher's exact test for categorical variables and Wilcoxon rank-sum test for continuous variables. Logistic regression models were used to identify factors associated with non-curative resection after ESD. Kaplan-Meier analysis and log-rank tests were used for survival analysis. The index date was defined as the date of the first procedure. The patients were followed up from the index date to the time of death or the last follow-up date until June 2018. Statistical significance was set at $p<0.05$. All statistical analyses were performed using R 3.5.1 (R Foundation, Vienna, Austria; https://www.R-project.org/).

Ethical statements

The Institutional Review Board (IRB) of Asan Medical Center approved this study (IRB No: 2018-0249). All patients provided informed consent before the procedure.

RESULTS

Baseline characteristics

The baseline characteristics of patients with cirrhosis are summarized in Table 1. The SENs of cirrhotic patients subjected to the procedure more than once were numbered in chronological order. Of the 15 cirrhotic patients with 17 SENs included in the analysis, 11 patients (73.3%) had early-stage cirrhosis classified as Child-Pugh class A. Three patients (20%) were classified as Child-Pugh class B and one patient (6.7%) as Child-Pugh class C. Excessive alcohol consumption (n=11, 73.3%) was the most common etiology of cirrhosis, followed by hepatitis B virus infection (n=3, 20%) and primary biliary cirrhosis (n=1, 6.7%).

The comparison between cirrhotic and non-cirrhotic patients did not show significant differences between the two groups regarding sex, age, smoking, and alcohol consumption status (Table 2). Factors influenced by cirrhosis itself or those associated with splenomegaly, including prothrombin time, albumin, bilirubin, and platelet count, were significantly different between the two groups.

Endoscopic and oncologic outcomes of ESD

The endoscopic outcomes of 17 SENs in 15 cirrhotic patients and 464 SENs in 422 non-cirrhotic patients are shown in Table 3. Although the lesion size tended to be smaller in cirrhotic patients (12.0 mm vs. 18.5 mm, p=0.065), the total procedure time (median 44 minutes vs. 40 minutes, p=0.367) and hemostasis time during the procedure (median 5 minutes vs. 5 minutes, p=0.152) were similar between the groups. *En bloc* resection, complete resection, and curative resection rates were comparable between the cirrhosis and non-cirrhosis groups.

Adverse events occurred in 61 cases (12.7%), including 11 bleeding (2.3%), 17 perforation (3.5%), and 33 stricture (6.9%). Bleeding was observed more frequently in the cirrhosis group than in the non-cirrhosis group (p=0.054). Seven patients (41.2%) in the cirrhosis group received fresh-frozen plasma transfusions before ESD. Furthermore, four patients (3 [17.6%] for cirrhosis and 1 [0.2%] for idiopathic thrombocytopenic purpura in the non-cirrhosis group) received platelet transfusion before ESD. All bleeding cases were successfully managed endoscopically without the need for additional surgery or angiography. Esophageal varices were documented in eight of 17 SENs in the cirrhosis group, and their characteristics are presented in Table 1. Severe bleeding from an esophageal varix was observed in one patient (SEN 7) during the ESD procedure. Resection

Table 1. Clinical characteristics of patients in the cirrhosis group

SEN no.	Patient no.	Sex	Age (yr)	Etiology of LC	C-P class (score)	INR	Platelet count (×1,000/mL)	Albumin (g/dL)	Bilirubin (mg/dL)	Ascites	Esophageal varix[a]	Lesion location	CuR	Reason for non-CuR	Adverse event
1	1	M	66	Alcohol	A (6)	0.98	158	3.3	0.8	None	No	Upper	Yes	-	Stricture
2	2	M	60	Alcohol	C (10)	1.31	93	2.7	3.6	Slight	F1CbLi	Middle	No	Piecemeal resection	-
3	3	M	71	HBV	A (6)	1.01	205	3.4	0.7	None	No	Lower	Yes	-	-
4	4	M	73	Alcohol	B (9)	1.08	143	2.7	1.6	Moderate	F2CbLi	Middle	Yes	-	Stricture
5	5	M	63	Alcohol	A (5)	1.06	126	3.9	0.6	None	F1CbLi	Lower	No	SMI (+)	-
6	5	M	68	Alcohol	A (5)	1.26	123	3.9	0.6	None	F1CbLi	Middle	Yes	-	-
7	6	M	56	Alcohol	B (7)	1.31	95	2.7	1.7	None	F1CbLm	Lower	No	LRM (+)	Varix bleeding
8	7	M	61	Alcohol	A (5)	1.22	100	3.7	0.5	None	F1CbLm	Lower	Yes	-	-
9	7	M	61	Alcohol	A (5)	1.17	101	3.8	0.7	None	F1CbLm	Middle	Yes	-	-
10	8	M	55	Alcohol	B (7)	1.09	162	2.5	0.9	None	No	Lower	Yes	-	-
11	9	F	75	PBC	A (5)	1.01	176	3.7	0.6	None	No	Middle	Yes	-	-
12	10	M	59	Alcohol	A (5)	0.92	179	3.9	1.8	None	No	Middle	No	LRM (+)	Bleeding
13	11	M	64	HBV	A (5)	1.01	142	3.8	0.6	None	No	Middle	Yes	-	-
14	12	M	57	HBV	A (5)	1.06	107	3.8	0.6	None	No	Lower	Yes	-	-
15	13	M	67	Alcohol	A (6)	1.1	154	3.5	0.7	None	No	Upper	Yes	-	-
16	14	M	64	Alcohol	A (5)	0.97	223	3.9	0.4	None	No	Middle	No	SMI (+)	-
17	15	M	68	Alcohol	A (6)	1.15	109	3.4	0.9	None	F1CbLi	Middle	No	SMI (+)	Stricture

SEN, superficial esophageal neoplasm; LC, liver cirrhosis; C-P, Child-Pugh; INR, international normalized ratio; CuR, curative resection; HBV, hepatitis B virus; SMI, submucosal invasion; LRM, lateral resection margin; PBC, primary biliary cirrhosis.
[a]Esophageal varices were assessed according to the general rules for recording endoscopic findings of esophagogastric varices.

Table 2. Baseline characteristics of all patients

Characteristic	Cirrhosis (*n*=17)	Non-cirrhosis (*n*=464)	*p*-value
Male sex	16 (94.1)	438 (94.4)	1.000
Age (yr)	64 (60–68)	65 (59–71)	0.551
Smoking			0.594
Current	6 (35.3)	120 (25.9)	
Past	9 (52.9)	255 (55.0)	
Never	2 (11.8)	89 (19.2)	
Alcohol consumption			0.517
Current	10 (58.8)	199 (42.9)	
Past	6 (35.3)	200 (43.1)	
Never	1 (5.9)	65 (14.0)	
Prothrombin time (INR)	1.08 (1.01–1.17)	0.98 (0.94–1.02)	<0.001
Albumin (g/dL)	3.7 (3.3–3.8)	3.9 (3.7–4.1)	<0.001
Bilirubin (mg/dL)	0.7 (0.6–0.9)	0.5 (0.4–0.7)	0.003
Platelet count (×1,000/mL)	142 (107–162)	216 (184–257)	<0.001
Creatinine (mg/dL)	0.83 (0.73–1.00)	0.90 (0.80–1.00)	0.188
Tumor location			0.686
Upper esophagus	2 (11.8)	36 (7.8)	
Middle esophagus	9 (52.9)	277 (59.7)	
Lower esophagus	6 (35.3)	151 (32.5)	

Values are presented as number (%) or median (interquartile range).
INR, international normalized ratio.

Table 3. Outcomes of endoscopic submucosal dissection

Outcome	Cirrhosis (*n*=17)	Non-cirrhosis (*n*=464)	*p*-value
Lesion size (mm)	12 (10–18)	18.5 (12–29)	0.065
Specimen size (mm)	29 (27–41)	35 (28–45)	0.115
Total procedure time (min)	44 (30–70)	40 (29–54)	0.367
Hemostasis time (min)	5 (4–10)	5 (3–7)	0.152
Circumference (%)			0.837
<50	11 (64.7)	258 (55.6)	
50–75	4 (23.5)	128 (27.6)	
>75	2 (11.8)	78 (16.8)	
Histology			0.382
Dysplasia	2 (11.8)	110 (23.7)	
Squamous cell carcinoma	15 (88.2)	354 (76.3)	
Histological depth of invasion			0.492
T0	2 (11.8)	110 (23.7)	
M1	5 (29.4)	114 (24.6)	
M2	4 (23.5)	140 (30.2)	
M3	3 (17.6)	53 (11.4)	
SM	3 (17.6)	47 (10.1)	
En bloc resection	15 (88.2)	450 (97.0)	0.105
Complete resection	14 (82.4)	415 (89.4)	0.413
Lymphovascular invasion	1 (5.9)	15 (3.2)	0.443
Curative resection	11 (64.7)	366 (78.9)	0.224
Adverse events			
Bleeding	2 (11.8)	9 (1.9)	0.054
Perforation	0	17 (3.7)	1.000
Stricture	3 (17.6)	30 (6.5)	0.103
Hospital stay duration (day)	5 (4–7)	5 (4–7)	0.794
Overall death	3 (17.6)	33 (7.1)	0.127

Values are presented as median (interquartile range) or number (%).
T0, dysplasia; M1, carcinoma *in situ*; M2, tumor invading the lamina propria; M3, tumor involving the muscularis mucosa; SM, tumor invading the submucosa.

was non-curative because poor visualization due to bleeding made it impossible to procure sufficient resection margins. In the non-cirrhosis group, 17 patients had perforation during the endoscopic procedure, and all recovered after several days of fasting with or without endoscopic closure. No patient required additional surgery or intervention to manage the perforation. Overall, post-ESD strictures occurred in 33 cases (6.9%) and showed no difference between the groups (p=0.103). Of these, 18 cases of stricture required endoscopic balloon dilatation and three required temporary stent insertion to manage luminal narrowing. In the cirrhosis group, one patient (SEN 4) underwent balloon dilatation and another patient (SEN 1) successfully underwent temporary stent insertion without adverse events. The remaining 1 cirrhotic patient with stricture was observed without intervention because the symptoms were not severe.

Curative resection was not achieved in six SENs in six cirrhotic patients and in 98 SENs in 95 non-cirrhotic patients for the following reasons: 50 submucosal invasion, 34 positive resection margins, 10 lymphovascular invasion, nine piecemeal resection, and one poorly differentiated histology. Of the six cirrhotic patients with non-curative resection, two patients underwent radiation therapy (RT), and the other four patients were observed without additional treatment due to old age or the patient's refusal to undergo treatment. During a median follow-up of 29.8 months (interquartile range [IQR], 12.8–60.8 months), there was one metachronous recurrence in the RT group, which was treated with an additional ESD (Fig. 1). Of the 95 non-cirrhotic patients who underwent non-curative resection, 20 patients underwent additional esophagectomy, 10 patients underwent concurrent chemoradiation therapy, and four patients underwent

RT (Supplementary Fig. 1). During the median follow-up period, there was one metachronous recurrence in the RT group, while no recurrences were observed in the esophagectomy and concurrent chemoradiation therapy groups. The remaining 61 patients were observed without additional treatment, and 10 recurrence cases were reported within the group. One synchronous recurrence was confirmed as local recurrence, and the patient underwent esophagectomy.

Overall, curative resection was achieved in 377 SENs in 349 patients. Of the 10 cirrhotic patients who underwent curative resection, two had synchronous recurrences, which were treated with additional EMR and ESD (Fig. 2). In the non-cirrhosis group, 21 patients with recurrence underwent additional sessions of ESD, four patients (including one patient with local recurrence) were treated with argon plasma coagulation, and one patient was treated with surgical esophagectomy (Supplementary Fig. 2). The median duration from ESD to recurrence was 14.8 months (IQR, 6.8–29.9 months).

Univariate logistic regression analysis, conducted to evaluate factors associated with non-curative resection, showed that lesion size, specimen size, and procedure time were related to non-curative resection (Table 4). Cirrhosis was not a significant risk factor for non-curative resection (p=0.171). In multivariate analysis, a longer procedure time was the only significant risk factor affecting non-curative resection (p=0.046).

Survival analysis revealed that the cirrhosis group showed a

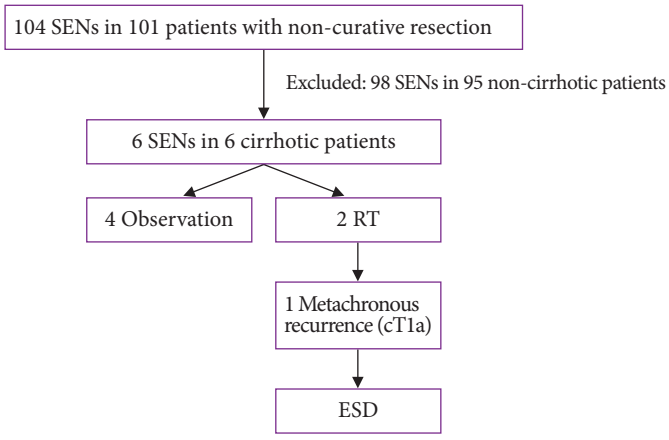

Fig. 1. Clinical course of cirrhotic patients with non-curative resection. SEN, superficial esophageal neoplasm; RT, radiation therapy; ESD, endoscopic submucosal dissection.

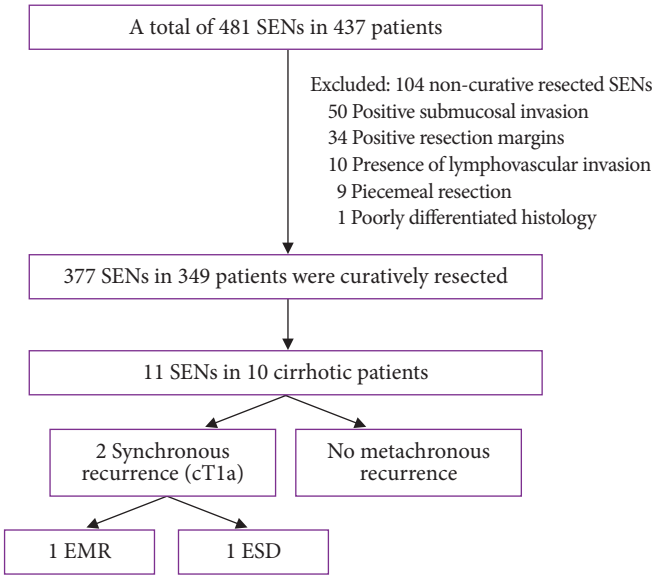

Fig. 2. Clinical course of cirrhotic patients with curative resection. SEN, superficial esophageal neoplasm; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.

Table 4. Factors associated with non-curative resection after endoscopic submucosal dissection (n=104)

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.002 (0.976–1.030)	0.867	-	-
Male sex	0.963 (0.401–2.684)	0.938	-	-
Tumor location				
Lower (reference)	1	-	-	-
Middle	1.043 (0.655–1.683)	0.861	-	-
Upper	0.678 (0.240–1.658)	0.424	-	-
Lesion size	1.018 (1.003–1.033)	0.020	1.002 (0.975–1.031)	0.875
Specimen size	1.020 (1.005–1.036)	0.010	1.008 (0.978–1.037)	0.599
Procedure time	1.011 (1.004–1.018)	0.002	1.008 (1.000–1.017)	0.046
Cirrhosis	2.037 (0.687–5.494)	0.171		

OR, odds ratio; CI, confidence interval.

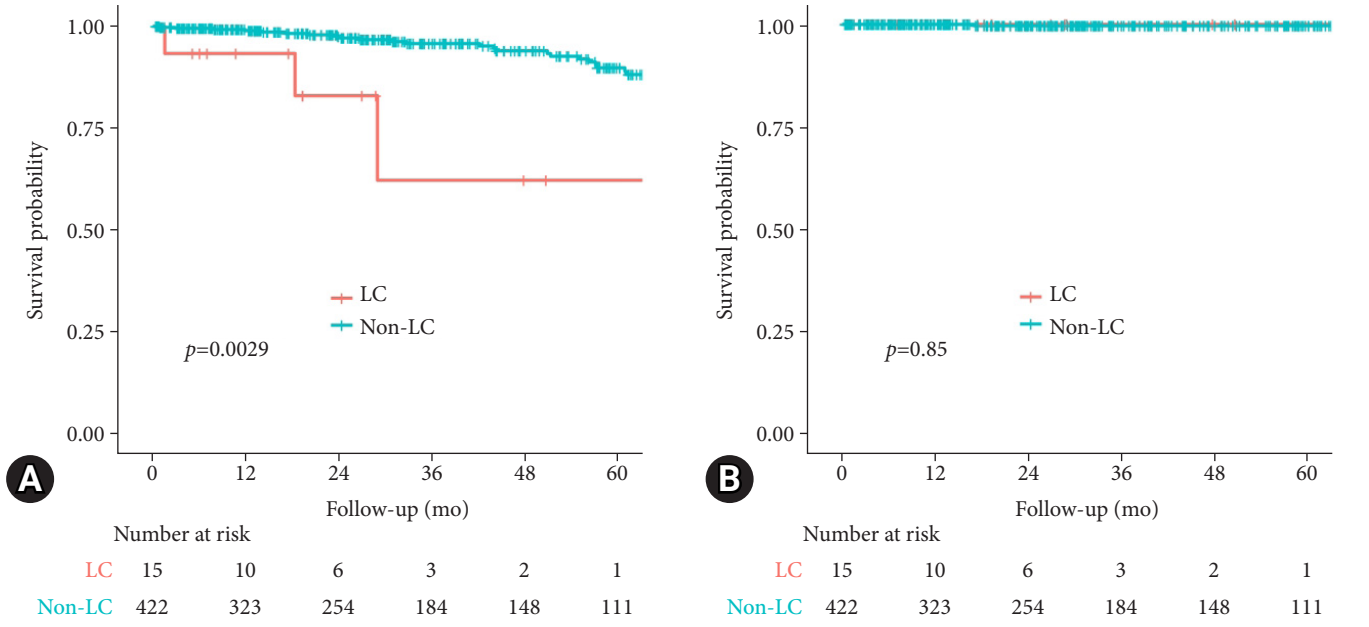

Fig. 3. (A) Overall survival after endoscopic submucosal dissection. (B) Disease-specific survival after endoscopic submucosal dissection. LC, liver cirrhosis.

poorer overall survival than the non-cirrhosis group after adjusting for the follow-up duration (p=0.003) (Fig. 3A), while disease-specific survival did not show a difference between the groups (p=0.85) (Fig. 3B). There was no periprocedural mortality caused by ESD itself. The median follow-up period was 19.3 months (IQR, 8.8–28.8 months) for the cirrhosis group and 30.4 months (IQR, 12.8–61.3 months) for the non-cirrhosis group.

None of the patients in the cirrhosis group experienced deterioration in liver function after ESD. Two patients showed an improvement in the Child-Pugh classification after ESD (SEN 2 from classification C to B and SEN 7 from classification B to A in Table 1); however, the improvement was transient as it was caused by fresh-frozen plasma transfusion and albumin replacement during the in-hospital period.

DISCUSSION

In this study, we compared the outcomes of esophageal ESD between cirrhotic and non-cirrhotic patients. The resection rates, including *en bloc* resection (88.2%), complete resection (82.4%), and curative resection (64.7%) in the cirrhosis group, were comparable to those of the non-cirrhosis group. This result was consistent with two previous studies that reported complete resection rates of 85.7% and 77.8%.[8,9] In addition to the fact that the cirrhosis group showed resection results comparable to those of the non-cirrhosis group, similar disease-specific survival in the two groups suggested that ESD could be an effective treatment option in cirrhotic patients with SENs.

As esophagectomy in patients with cirrhosis carries a high risk of morbidity and mortality,[7,15] ESD could be a better option than surgery in patients with both liver cirrhosis and SENs. However, as cirrhotic patients are well known to have a bleeding tendency and vulnerability to infection, there are concerns about increased postprocedural adverse events in cirrhotic patients. In the case of gastric ESD, which has been investigated more than esophageal ESD, a recent study has reported that performing gastric ESD in patients with compensated cirrhosis showed feasible efficacy and safety compared with that in non-cirrhotic patients without high risk of bleeding.[16] On the contrary, the present study, which evaluated the outcomes of esophageal ESD, demonstrated that bleeding events were more frequent in the cirrhosis group (p=0.054), although the lesion size tended to be smaller in the cirrhosis group (p=0.065). This discrepancy in the risk of bleeding between gastric and esophageal ESD in cirrhotic patients could be explained by two factors. First, the present study included more patients with advanced cirrhosis than previous studies on gastric ESD.[16] Second, the presence of esophageal varix was another reason because varices serve as an obstacle in performing esophageal ESD in cirrhotic patients and sometimes cause serious bleeding.

In the present study, bleeding was observed more frequently in the cirrhosis group than in the non-cirrhosis group, and other adverse events, including perforation and strictures, were not different between the groups. Of the bleeding patients in the cirrhosis group, eight of 17 cases had concurrent esophageal varices, and there was one case of severe variceal bleeding during the ESD procedure for which curative resection could not be achieved. Taken together with the fact that all bleeding events were controllable with endoscopic hemostasis without further adverse events, and none of the cirrhotic patients experienced deterioration of liver function after the procedure. We expected this was due to careful and intensive hemostasis during the procedure. Therefore, a meticulous evaluation of the spatial relationship between esophageal varix and neoplasm and through hemostasis should be performed before and during ESD. Moreover, performing endoscopic variceal ligation before ESD may be helpful in some cases.[8,9]

The curative resection rate in the cirrhosis group was 64.7% in our study, which was not as high as that of the non-cirrhosis group. There were six cases of non-curative resection in the cirrhosis group: three SM invasions, one piecemeal resection, and two lateral margin involvement. Of these, five cases, including three SM invasions, one piecemeal resection, and one lateral margin involvement, were caused by tumor factors or technical problems, and were not related to the underlying cirrhosis. The other patient with lateral margin involvement was the only patient affected by underlying cirrhotic conditions of bleeding with poor visualization. Of these non-curative resection patients, two patients underwent additional RT, and four patients were closely observed. During the median follow-up period, one patient in the RT group had a metachronous recurrence of mucosal cancer and no recurrence in the observation group. The disease-specific survival rate between patients with and without cirrhosis was not different. Considering the fact that esophagectomy is associated with a high morbidity rate of 83%–87% and mortality rate of 17%–30%, ESD followed by additional therapy, such as RT or concurrent chemoradiation therapy, could be considered carefully as an alternative therapy for esophageal cancer with submucosal invasion in patients with cirrhosis.[17]

This study has several limitations. First, although this study included the largest number of cirrhotic patients thus far reported to our knowledge, there were only 17 cases in the cirrhosis group, and all ESD procedures were performed in a single center. As a result, definitive conclusions cannot be drawn. Second, as a limitation of the retrospective study design, other comorbidities, including coagulopathy and the use of antithrombotic agents, which may be confounding factors, were not adequately investigated. Third, ESD is an endoscopist-dependent procedure, and candidates for ESD were selected based on the discretion of the endoscopist. Therefore, a selection bias may have been present. However, our study showed favorable outcomes of ESD for SENs in patients with cirrhosis during a long-term follow-up period.

In conclusion, we propose that ESD could be a safe and effective treatment option for SENs in patients with cirrhosis. Before performing esophageal ESD in cirrhotic patients, a detailed preprocedural assessment, including assessment of the esophageal varix status and the remaining life expectancy, is needed to select patients with the greatest benefit.

Supplementary Material

Supplementary Fig. 1. Clinical course of non-cirrhotic patients with non-curative resection.

Supplementary Fig. 2. Clinical course of non-cirrhotic patients with curative resection.

Supplementary materials related to this article can be found online at https://doi.org/10.5946/ce.2021.242.

Conflicts of Interest

The authors have no potential conflicts of interest.

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Author Contributions

Conceptualization: YKC, JHN, DHK; Data curation: YKC, JHN, DHK, HKN, JYA, JHL, KWJ, KDC, HJS, GHL, HYJ; Formal analysis: YKC, JHN, DHK; Methodology: YKC, JHN, DHK; Supervision: DHK; Writing–original draft: YKC, JHN, DHK; Writing–review & editing: YKC, JHN, DHK, HKN, JYA, JHL, KWJ, KDC, HJS, GHL, HYJ.

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