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의학석사학위논문

대장종양절제시 점막하박리술과 점막하박리술-
올가미병용절제술의 장기예후비교

Long-term clinical outcomes of endoscopic submucosal
dissection for colorectal neoplasia with or without the hybrid
technique

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의학과

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submucosal dissection for colorectal neoplasia
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이 논문을 의학석사학위논문으로 제출함

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English Abstract

Background and aims:

Few studies have addressed the long-term outcomes of hybrid endoscopic submucosal dissection (ESD-H) in the colorectum. We did so in our current study in comparison with a conventional colorectal ESD approach in which submucosal dissection was continued throughout, until the completion of resection (ESD-T).

Method: The medical records of 836 colorectal neoplasia patients treated by ESD-T or ESD-H were reviewed retrospectively. ESD-H was defined as colorectal ESD with additional snaring in the final stage of the procedure. Primary outcomes were the overall and metastatic recurrence rates. Secondary outcomes were short-term outcomes such as the en bloc resection rate, procedure time and adverse events.

Result: The overall recurrence rate was higher in the ESD-H than in the ESD-T group (5.7% vs 0.7%, $p = 0.001$). The metastatic recurrence rate showed no significant difference between these groups (1.4% vs 1.4%, $p = 1.000$). Multivariate analysis revealed that a failed en bloc resection (HR 24.097, 95% CI 5.446-106.237; $p < 0.001$) and larger tumor size (HR 1.042 95% CI 1.014-1.070; $p = 0.003$) were independently associated with overall recurrence. The ESD-H group showed a lower en bloc resection rate (56.8% vs 96.5%, $p < .001$), shorter procedure time (45.6 vs 54.3 min, $P < .001$) and higher perforation rate (10.3% vs 6.0%, $p = .029$).

Conclusion: Although long-term outcomes in terms of overall recurrence are inferior following ESD-H, a failed en bloc resection and large tumor size are the only independent risk factors for recurrence. Further investigations are warranted to improve the long-term outcomes of ESD-H.

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Introduction

Endoscopic submucosal dissection (ESD) of the colorectum has a high possibility of achieving a successful en bloc resection regardless of tumor size. This method is therefore generally used for the resection of large tumors, particularly for removing suspected superficial submucosal cancers that cannot be removed en bloc using conventional endoscopic resection methods.¹⁻⁴ Despite its advantageous high en bloc resection rate, colorectal ESD has not yet been widely adopted in daily clinical practice because of its technical difficulty, long procedure time and high perforation rate.⁵⁻⁷ To overcome the high technical requirements of colorectal ESD, various modified approaches have been attempted such as hybrid ESD (ESD-H). In this hybrid method, standard submucosal dissection is initially performed using endoknives and snare resection of the undissected, narrowed submucosal tissue is added at the final stage of the procedure.

Many previous studies have compared the clinical outcomes of ESD-H with the conventional ESD approach in which submucosal dissection is continued throughout until completion of the tumor resection (ESD-T). In these prior studies, ESD-H showed a shorter procedure time than ESD-T.⁸⁻¹⁴ In general however, ESD-H has shown slightly lower en bloc and R0 resection rates, although several reports demonstrated similar rates between these procedures.^{1,8,12,15} Notwithstanding our increased understanding of these procedural characteristics from the perspective of short-term clinical outcomes, the clinical indications and usefulness of each procedure still requires clarification. This is because few studies to date have addressed the long-term outcomes of ESD-H in comparison to ESD-T such as the probability of residual lesions and/or recurrences. The purpose of our current study was to do this comparative analysis.

Materials and methods

Study population

In a retrospective analysis of the colorectal ESD database at Asan Medical Center, Seoul, Korea, 856 consecutive patients were found to have undergone colorectal ESD between 2005 and 2014. After excluding cases of neuroendocrine tumors and non-neoplastic polyps, we enrolled 836 lesions in the final analysis. All ESD procedures had been performed by 4 endoscopists (J.S.B., D.H.Y., B.D.Y., and K.J.K.) who were highly experienced in diagnostic and therapeutic colonoscopies including colorectal ESD. This study was approved by our Institutional Review Board (No. 2016-0967).

ESD procedures

All colorectal ESD procedures were performed under conscious sedation with midazolam and pethidine. A single-channel endoscope (GIF-H260, GIF-Q260J, and CF-H260; Olympus Co, Tokyo, Japan) was used. The endoknives used for mucosal incision and submucosal dissection included a flex knife (Olympus Co, Tokyo, Japan), fixed flexible snare knife (Kachu Technology Co, Seoul, Korea), and dual knife (Olympus Co, Tokyo, Japan). Colorectal ESD types were divided into two categories: 1) ESD-T in which submucosal dissection was continued until the completion of resection of a tumor, and 2) ESD-H in which submucosal dissection was performed initially and snare resection was added to grasp and remove the narrowed undissected portion of a tumor in the final stage of the procedure. The detailed procedural steps for ESD-T are described in our previous report.¹² The choice between ESD-T and ESD-H was made at the endoscopist's discretion. The main indications for ESD-H were 1) a benefit from a rapid completion of the resection procedure and 2) for use as a rescue procedure in cases where submucosal dissection could not be completed because of technical difficulties.

Histopathological evaluation

The lesions in the study population were grossly classified as a sessile tumor or laterally spreading tumor (LST). According to the Paris classification, the sessile type indicates a tumor with a 0-Is appearance.¹⁶ The LST lesions were further subdivided into granular (LST-G) and non-granular type (LST-NG).^{16,17} All specimens were fixed in formalin and serially sectioned at 2 mm intervals to assess tumor involvement at the lateral and vertical margins. Tumor size and histopathology were evaluated by board-certified gastrointestinal pathologists. Histologic diagnoses were based on the World Health Organization criteria.¹⁸

Outcome parameters

The long-term clinical outcomes were the primary interest of this present study and recurrence was the main outcome parameter. Recurrences were classified as local or metastatic. A local recurrence was defined as a recurred tumor at the ESD site. Metastatic recurrences were defined as a metastasis to the lymph nodes and/or distant organs such as liver and lung after ESD treatment of a colorectal cancer.

The secondary endpoints of this current study were the short-term outcomes of the colorectal ESD procedures, which included en bloc resection, R0 resection, curative resection, procedure time, and procedure-related adverse events. En bloc resection was defined as resection in a single piece. R0 resection was defined as an en bloc resection with free lateral and vertical resection margins. Curative resection was defined as an R0 resection with no unfavorable histological features such as a deep submucosal cancer invasion >1,000 µm from the muscularis mucosa, lymphovascular invasion, poor differentiation, or tumor budding. The procedure time was defined as the time from the beginning of the submucosal injection to complete removal of the tumor. Delayed bleeding was defined as any bleeding necessitating emergency department presentation, hospitalization, or re-intervention (repeat colonoscopy with or without endoscopic hemostasis, angiography or surgery) after

completion of the ESD procedure.

Surveillance endoscopy and imaging

The first surveillance endoscopy (sigmoidoscopy and/or colonoscopy) was performed approximately 1 year after the R0 resection but at around 6 months in cases of piecemeal resection or a histologically positive resection margin. The intervals for subsequent surveillance endoscopies were individualized in accordance with the first surveillance endoscopy findings. Local recurrence was confirmed by histological examination of biopsied tissue. Radiological imaging studies were performed regularly after ESD interventions for early colorectal cancers. Abdominopelvic and chest CT scans were conducted annually up to 5 years post-surgery. These intervals were shortened if clinically indicated.

Statistical analysis

Data were reported as means with standard deviations. Medians were reported with ranges including the values of the interquartile range (IQR). Continuous parameters were analyzed using a Student's t-test or the Mann-Whitney U test, whereas categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. P values of less than 0.05 in a two-sided test were considered statistically significant. Cumulative overall and metastatic recurrence rates were analyzed with the Kaplan–Meier method. Comparisons of overall and metastatic recurrence rates were performed with the log rank test. To examine risk factors for recurrence, a Cox proportional hazards model was used in the univariate and multivariate analyses. When the variables in the univariate analysis were statistically significant, multivariate analysis was performed with backward elimination. All statistical analyses were performed using SPSS version 20 software (SPSS Inc., Chicago, IL).

Results

Baseline characteristics of the study patients

Of the 836 colorectal cancer cases included in this analysis, 563 patients underwent ESD-T and 273 underwent ESD-H. The baseline characteristics of the whole cohort are presented in Table 1. The mean age and gender distribution were similar between the ESD-T and ESD-H groups. However, the mean tumor size was smaller in the ESD-H group (27.9 ± 13.7 vs 33.2 ± 16.2 mm; $p < .001$). The proportion of submucosal cancers was higher in the ESD-H group (Table 1).

Table 1. Baseline characteristics of the included colorectal ESD patients (n=836)

	ESD-T	ESD-H	<i>P value</i>
	n=563	n=273	
Age, mean (SD), years	61.7±9.7	61.8±10.1	0.933
Sex, no. (%)			0.592
Male	347 (61.6%)	163 (59.7%)	
Female	216 (38.4%)	110 (40.3%)	
Tumor size, mean (SD)	33.2±16.2	27.9±13.7	<0.001
Morphology, no. (%)			0.141
Sessile	127 (22.6%)	76 (27.8%)	
LST-G	115 (20.5%)	44 (16.1%)	
LST-NG	320 (56.9%)	153 (56.0%)	
Location, no. (%)			0.168
Rectum	274 (48.7%)	119 (43.6%)	
Above rectum	289 (51.3%)	154 (56.4%)	

Cecum	14 (4.8%)	9 (5.8%)
Ascending colon	89 (30.8%)	50 (32.5%)
Transverse colon	79 (27.3%)	28 (18.2%)
Descending colon	21 (7.3%)	11 (7.1%)
Sigmoid colon	86 (29.8%)	56 (36.4%)
Histology, no. (%)		<0.001
Adenoma	357 (63.4%)	135 (49.5%)
M	126 (22.4%)	64 (23.4%)
Superficial SM*	46 (8.2%)	33 (12.1%)
Deep SM**	33 (5.9%)	37 (13.6%)
SM unknown	1 (0.2%)	4 (1.5%)

ESD endoscopic submucosal dissection; *ESD-T* throughout *ESD*; *ESD-H* hybrid *ESD*; *LST-G* laterally spreading tumor granular type; *LST-NG* laterally spreading tumor nongranular type; *M* mucosa; *SM* submucosa;

*Superficial submucosal cancer invasion was defined as $\leq 1,000$ μm from the muscularis mucosa.

**Deep submucosal cancer invasion was defined as $> 1,000$ μm from the muscularis mucosa.

Comparison of short-term outcomes between the procedures

The *ESD-H* group showed lower en bloc resection (56.8% vs 96.5%, $P < .001$), R0 resection (46.2% vs 78.5%, $P < .001$) and curative resection rates (38.1% vs 73.5%, $P < .001$). the incidence of delayed bleeding was comparable in both groups but the perforation rate was higher in the *ESD-H* group (10.3% vs 6.0%, $p = .029$). The procedure time was shorter in the *ESD-H* group (45.6 ± 40.8 vs 54.3 ± 46.5 min, $P < .001$). Table 2 summarizes these short-term outcomes in both groups.

Table 2. Short term outcomes of ESD-T and ESD-H

		ESD-T	ESD-H	P value
		n=563	n=273	
En bloc resection, no. (%)	Success	543 (96.5%)	155 (56.8%)	<.0001
Complete resection, no. (%)	Success	442 (78.5%)	126 (46.2%)	<.0001
Curative resection, no. (%)	Success	414 (73.5%)	104 (38.1%)	<.0001
Delayed bleeding, no. (%)	Occurred	11 (2.1%)	4 (1.9%)	0.913
Perforation, no. (%)	Occurred	34 (6.0%)	28 (10.3%)	0.029
	Medical treatment	33 (97.1%)	28 (100.0%)	1
	Surgical treatment	1 (1.9%)	0 (0.0%)	
Procedure time, mean (SD), min		54.3 (46.5%)	45.6 (40.8%)	<.0001

ESD endoscopic submucosal dissection; *ESD-T* throughout ESD; *ESD-H* hybrid ESD;

Comparison of long-term outcomes between the procedures

Of the 563 patients in the ESD-T group, additional surgical colorectal resection was performed in 40 cases. This intervention was needed due to unfavorable histological features with or without incomplete resection in 30 patients and because of an incomplete resection in 10 patients (Fig. 1). Chemoradiation therapy was also required in one patient because of unfavorable histological features. It was noted that 109 of 563 patients in the ESD-T group were lost to follow-up. Among the 273 patients in the ESD-H group, additional surgery was performed in 55 cases. This was due to unfavorable histological features with or without incomplete resection in 39 patients and because of an incomplete resection in 16 cases. Chemoradiation was also required in one patient in this group because of unfavorable

histological features. Forty-three patients in the ESD-H group were lost to follow up.

We finally analyzed the long-term outcomes of 413 ESD-T patients over a median follow-up of 30 months (IQR, 12-55 mos) and 174 ESD-H patients with a median follow-up of 31 months (IQR, 12-57.3 mos) (Fig. 1). The average numbers of surveillance endoscopies during these follow-up periods were 2.5 ± 1.6 and 2.7 ± 1.8 in the ESD-T and ESD-H groups, respectively. The overall recurrence rate during the follow-up period was higher in the ESD-H group (10/174, 5.7% vs 3/413, 0.7%; $p = 0.001$). Detailed clinical features of these recurrences are presented in Table 3. A Kaplan-Meier curve revealed a significantly higher cumulative overall recurrence in the ESD-H group (Fig. 2). Of the patients with early colorectal cancer who were followed-up without additional surgery or chemoradiation, metastatic recurrence developed in 2 of 145 patients in the ESD-T group and in 4 of 73 patients in the ESD-H group (1.4% vs 5.5%, $p = 1.000$). The cumulative metastatic recurrence rate showed no significant difference (Fig. 3).

Table 3. Clinical characteristics of the recurrences in the study population

No.	ESD type	Age	Tumor size (mm)	Morphology	Histology	En bloc resection	Curative resection	Time to recurrence (months)	Histology of recurrent lesions	Management of recurrent lesions
1	ESD-T	81	60	Sessile	Adenoma	No	No	50	Adenoma	EMR, APC
2*	ESD-T	50	15	LST-NG	Deep SM	Yes	No	17	LN	Surgery
3	ESD-T	67	90	LST-G	M	Yes	Yes	17	Lung metastasis	Chemotherapy
4	ESD-H	65	20	LST-NG	M	No	No	35	Adenoma	F/U Loss
5	ESD-H	49	15	Sessile	SM unknown	No	No	81	Adenoma	EMR, APC
6	ESD-H	62	20	Sessile	Adenoma	No	No	6	Adenoma	F/U Loss
7	ESD-H	55	50	Sessile	Adenoma	No	No	48	Adenoma	APC
8	ESD-H	63	65	LST-G	M	Yes	No	31	Liver metastasis	Surgery with chemotherapy
9	ESD-H	78	50	LST-G	M	No	No	16	Adenoma	EMR, APC
10	ESD-H	55	20	LST-NG	Adenoma	No	No	40	Adenoma	ESD
11	ESD-H	66	40	LST-G	Adenoma	No	No	52	Adenoma	EMR, APC
12	ESD-H	66	50	LST-G	Adenoma	No	No	27	Adenoma	EMR, APC
13	ESD-H	58	40	Sessile	Adenoma	No	No	13	Adenoma	EMR

ESD, endoscopic submucosal dissection; *ESD-T*, throughout ESD; *ESD-H*, hybrid ESD; *LST-G*, laterally spreading tumor granular type; *LST-NG*, laterally spreading tumor nongranular type; *SM*, submucosa; *LN*, lymph node; *EMR*, endoscopic mucosal resection, *APC*, argon plasma coagulation; *F/U*, follow-up.

*This patient had liver cirrhosis and a double primary tumor including rectal cancer and hepatocellular carcinoma at the right hepatic lobe. Because the surgical risk was high and a cure was possible via ESD for the rectal cancer and radiofrequency ablation for hepatocellular carcinoma, non-surgical treatment with close monitoring at follow-up was selected as the long-term management plan.

Factors affecting overall recurrence

By univariate analysis, we found that the factors associated with overall recurrence were the ESD-H procedure (hazard ratio (HR) 6.431, 95% confidence interval (CI) 1.738-23.801; $p = 0.005$), a larger tumor size (HR 1.024, 95% CI 1.003-1.045; $p = 0.024$), a failed en bloc resection (HR 15.223, 95% CI 4.113-56.069; $p < 0.001$), a failed complete resection (HR 12.623, 95% CI 2.788-57.149; $p = 0.001$), delayed bleeding (HR 3.692, 95% CI 1.111-12.265; $p = 0.033$) and perforation (HR 4.317, 95% CI 1.160-16.058; $p = 0.029$). By multivariate analysis, a failed en bloc resection (HR 24.097, 95% CI 5.446-106.237; $p < 0.001$) and larger tumor size (HR 1.042 95% CI 1.014-1.070; $p = 0.003$) were found to be independent risk factors for overall recurrence (Table 4).

Table 4. Risk factors for recurrence analyzed by Cox proportional hazards model (overall recurrence=13/587)

		Univariate				Multivariate			
		Hazard Ratio	95% CI		P value	Hazard Ratio	95% CI		P value
Group	ESD-H	6.431	1.738	23.801	.005				
Age, years		1.043	.980	1.110	.186				
Sex	Female	1.542	.496	4.795	.454				
Tumor location	Above rectum	1.138	.382	3.388	.817				
Histology	Adenoma	1.000			.609				
	M	1.159	.336	4.006	.815				
	Superficial SM	.000	.000	.	.985				
	Deep SM	5.212	.636	42.721	.124				
	SM unknown	2.596	.147	45.951	.515				
Tumor size		1.024	1.003	1.045	.024	1.042	1.014	1.070	.003
Morphology	Sessile	1.000			.145				
	LST-G	1.612	.433	6.006	.477				
	LST-NG	.383	.086	1.715	.210				
Complete resection	Failed	12.623	2.788	57.149	.001				
En bloc resection	Failed	15.223	4.133	56.069	< 0.001	24.097	5.466	106.237	< 0.001
Delayed Bleeding	Occurred	3.692	1.111	12.265	.033				
Perforation	Occurred	4.317	1.160	16.058	.029				
Procedure time, minutes		1.005	.997	1.012	.218				

ESD endoscopic submucosal dissection; *ESD-H* hybrid ESD; *LST-G* laterally spreading tumor granular type; *LST-NG* laterally spreading tumor nongranular type; *SM* submucosa

Discussion

In our present large scale retrospective review of patients who underwent colorectal ESD, the ESD-H surgery showed a shorter procedure time with lower en bloc, R0 and curative resection rates in terms of short-term outcomes. In terms of long-term clinical outcomes, ESD-H was associated with a higher recurrence rate compared to ESD-T. However, we found by multivariate analysis that the ESD-H method was not an independent risk factor for a higher recurrence rate. A failed en bloc resection and larger tumor size were revealed to be independent risk factors for overall recurrence after colorectal ESD.

Previous large-scale meta-analyses of colorectal ESD have reported relatively lower en bloc (68.4%; 95% CI, 51.7-81.3%) and R0 (60.6%; 95% CI, 40.6-77.5%) resection rates after ESD-H in comparison to those after ESD-T (91.0%; 95% CI, 89.2-92.5% and 82.9%; 95% CI, 80.4-85.1%, respectively).^{1,8,12,15} The en bloc and R0 resection rates associated with ESD-H in our current study series were 56.8% and 46.2%, respectively, which fall within the 95% CI of previous studies. The corresponding rates for ESD-T in our current patients were 96.5% and 78.5%, respectively. However, despite the inferior short-term outcome performance of ESD-H described in most previous reports,^{1,8,12,15} and also found in our present analysis, our previous prospective randomized trial showed similar short-term clinical outcomes between ESD-T and ESD-H. In that randomized controlled study, we found that the en bloc and R0 resection rates of ESD-H were 94.1% and 91.2%, respectively, which were comparable to the 100% and 93.5% rates found with the ESD-T cases.¹¹ Although the reason for this discrepancy between these studies is not readily clear, there are several plausible explanations. First, the ESD-H technique has not been yet standardized and the degree of submucosal dissection and optimal timing of snaring is likely to differ between studies, resulting in different outcomes. In our previous randomized trial, we devised an optimized ESD-H technique for complete, effective snaring of sufficiently narrowed undissected submucosal tissue. We believe that this technical refinement may have improved the en bloc and R0 resection rates. Second, because of its technical simplicity, ESD-H could have been

chosen as the rescue method for difficult lesions that the ESD-T approach failed to completely resect in the cohorts of previous retrospective studies. The inclusion of such difficult cases may have lowered the en bloc and R0 resection rates by ESD-H. This possibility is supported by our present study which included a higher proportion of early cancers in the ESD-H group (50.5%) compared to the ESD-T group (36.6%) and found lower en bloc and R0 resection rates in the ESD-H group. In comparison, our previous randomized trial included similar proportion of early cancers in both groups and observed similar en bloc and R0 resection rates.¹¹ Finally, because of its relative technical ease, ESD-H may have been performed more frequently by less experienced endoscopists, or at an earlier stage in the ESD career of these clinicians, in previous retrospective cohorts. This might be related to the lower en bloc and R0 resection rates previously reported for ESD-H patients. All these aforementioned factors may have contributed to discrepancies between prior studies on the en bloc and R0 resection rates associated with ESD-H.

The long-term clinical outcomes of ESD-H and ESD-T were evaluated with respect to the recurrence rate in our present study. The overall recurrence rate was significantly higher in the ESD-H group and most were local recurrences. We speculate that this higher recurrence rate may be related to the lower en bloc resection rate, i.e. the higher probability of piecemeal resection by ESD-H compared to ESD-T. However, this interpretation should be made cautiously because, as discussed earlier, the lower en bloc resection rate of ESD-H in our present study and other previous studies is debatable. Factors such as the use of ESD-H as a rescue method, the current lack of any standardized ESD-H technique, and possible preferences for this technically easier procedure by less experienced endoscopists can be associated with a lower en bloc resection rate of ESD-H. The en bloc and R0 resection rates may in fact become similar between ESD-H and ESD-T if a technically standardized and optimized ESD-H method is performed as a primary treatment option by experienced endoscopists. This, theoretically, could result in a similar local recurrence rate as a long-term outcome between ESD-H and ESD-T. Notably in this regard, our present multivariate analysis indicated that a failed en

bloc resection was an independent risk factor for overall recurrence whereas ESD-H was not, suggesting that the procedure itself is not the most important factor associated with the long-term clinical outcomes in these patients. Therefore, if we consider the long-term outcome of all ESD-H cases in current real-world practice, the recurrence rate may be higher than that of ESD-T. However, the long-term outcomes of non-rescue cases undergoing an optimized ESD-H by experienced endoscopists should be investigated further to verify this. The necessity of further studies can be also supported by several previous reports of a similar recurrence rates between ESD-T and modified ESD techniques. For example, a previous study which compared ESD-T and precut endoscopic mucosal resection (EMR-P) described statistically similar recurrence rates between EMR-P (2/257, 3.2%) and ESD-T (2/64, 0.8%).¹⁵ Another study which compared EMR-P, ESD-H, and ESD-T in 206 colorectal lesions also found no significant differences in the recurrence rates (0/91 [0%] in EMR-P, 0/57 [0%] in ESD-H, and 1/58 [1.7%] in ESD-T, respectively).⁸

We investigated the risk factors for recurrence by multivariate analysis because some baseline characteristics such as tumor size and histology differed between our ESD-H and ESD-T groups. A failed en bloc resection and larger tumor size were revealed as independent risk factors for recurrence. Several previous studies have also reported failed en bloc resection as a significant risk factor for recurrence after ESD.^{3,19} In addition, a tumor size above 4 cm has been found to be an independent risk factor for recurrence in previous studies, although these reports analyzed EMR and not ESD.^{19,20} Because ESD-H shares the technical features of snaring with EMR, tumor size could have been an independent risk factor when ESD-H was performed. In addition, a large tumor size extends the ESD-T procedure time, which could theoretically lower the endoscopist's attention to the procedure as time goes on. Such a lack of attention may be related to failed en bloc resection even in ESD-T, which can result in a higher recurrence rate.⁸

Most local recurrences after ESD can be successfully managed by endoscopic interventions such as EMR and/or argon plasma coagulation (Table 3). We therefore suggest that the long-term clinical outcomes in colorectal cancer patients

undergoing these surgeries, as determined by local recurrence rates, will be favorable and comparable with either ESD-H or ESD-T.

The present study had several limitations of note. First, because of the retrospective observational design of the analysis, some baseline characteristics were different between the ESD-H and ESD-T groups. Second, the indications and techniques associated with ESD-H were not standardized among the analyzed patients, which could have affected the observed outcomes. In daily clinical practice however, ESD-H can be attempted in various situations such as a rescue treatment for difficult lesions and for rapid completion in less complicated cases. Our present study may thus correctly represent the real-world outcomes of ESD-H. Finally, the follow-up period in our current study series was insufficient and longer follow-up studies of the long-term outcomes of ESD-H in the colorectum are warranted in the future.

In conclusion, ESD-H shows a shorter procedure time than ESD-T but in terms of short-term outcomes is associated with lower en-bloc and R0 resection rates than the conventional approach. Although ESD-H patients also appear to show a higher recurrence rate as a long-term outcome, this procedure is not an independent risk factor for recurrence. Failed en bloc resection and a large tumor size are the only significant risk factors of recurrence regardless of the ESD procedure. Further investigations are warranted to standardize the ESD-H technique to improve its long-term clinical outcomes.

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Figures

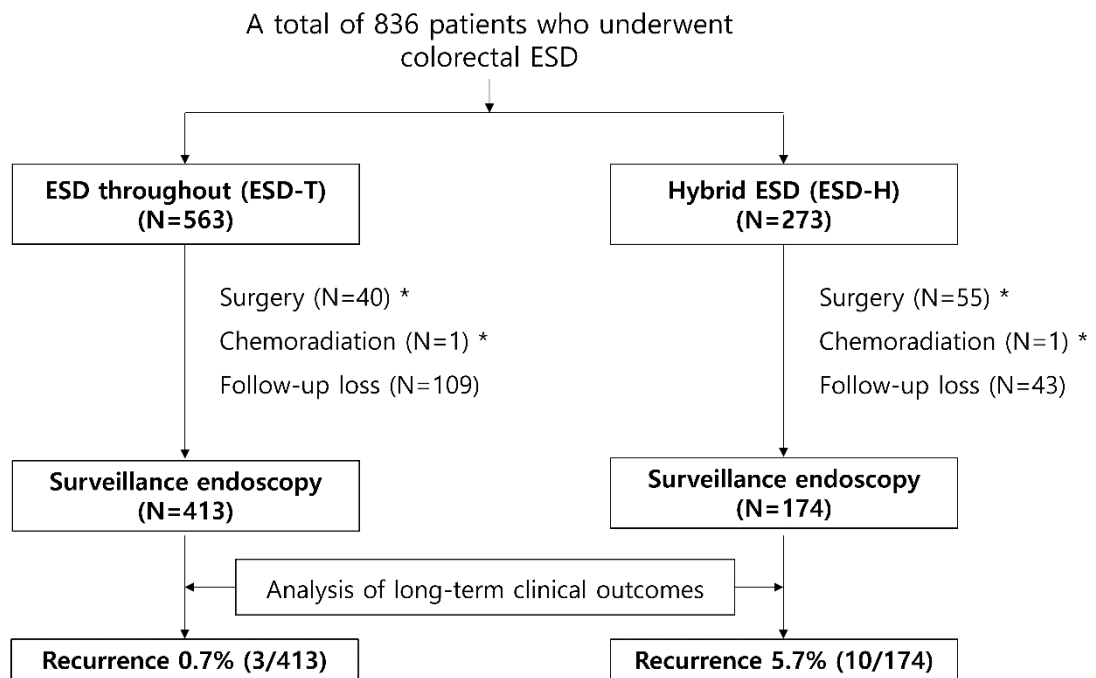


Figure 1. Flow chart showing the clinical courses among the study population

*Patients underwent additional surgery or chemoradiation because of unfavorable histological features or unfavorable histological features with incomplete resection.

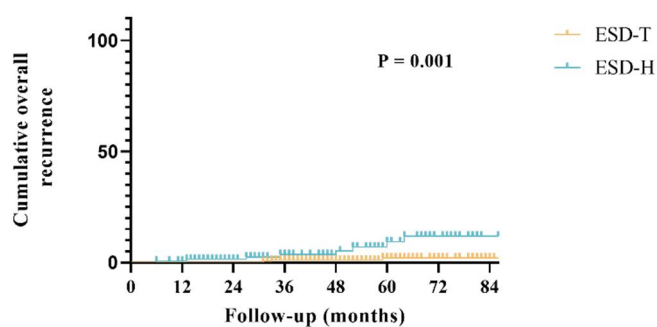


Figure 2. Cumulative overall recurrence rates after endoscopic treatment (Kaplan–Meier method)

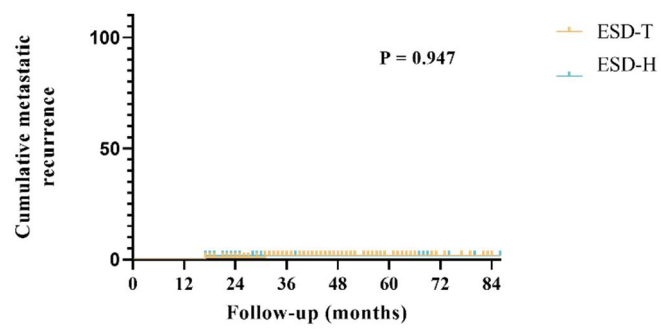


Figure 3. Cumulative metastatic recurrence rates after endoscopic treatment (Kaplan–Meier method)

국문 요약

배경/목표

대장선종 및 일부 조기 대장암의 치료에 점막하박리술이 이용되고 있으나 기술적 어려움과 시술시간이 긴 단점이 있다. 이를 보완하기 위해 여러 가지 시도가 있었으며 점막하박리술-올가미병용절제술도 그 한 방법이다. 이 절제법은 기술적으로 용이하여 시술시간을 줄일 수 있다는 장점이 있다. 그러나, 점막하박리술-올가미병용절제술 후 재발 등 장기 예후가 기존 점막하박리술에 비해 어떤지 비교한 연구는 부족하다. 따라서, 이 연구에서는 대장종양 절제 시 기존 점막하박리술과 점막하박리술-올가미병용절제술의 장기 예후를 비교, 분석하고자 하였다.

방법

2005년부터 2014년까지 기존 점막하박리술 또는 점막하박리술-올가미병용절제술을 받은 836명 환자들의 의무기록을 후향적으로 조사하였다. 점막하박리술-올가미병용절제술은 점막하박리술 시행하다가 완전 절제 전 남은 일부 점막하조직을 올가미로 죄어 절제한 경우로 정의하였다. 연구의 일차 목표는 장기 예후인 전체 재발률과 전이성 재발률을 비교하는 것이었으며, 이차 목표는 단기 성적인 일괄 절제율, 시술시간, 합병증 발생률을 비교하는 것이었다.

결과

전체 재발률은 점막하박리술-올가미병용절제술 군에서 더 높았다(5.7% vs 0.7%, $p = 0.001$). 전이성 재발률은 두 군에서 유의한 차이가 없었다(1.4% vs 1.4%, $p = 1.000$). 다변량 분석에서 일괄 절제에 실패한 경우(HR 24.097, 95% CI 5.446-106.237; $p < 0.001$)와 종양의 크기(HR 1.042 95% CI 1.014-1.070; $p = 0.003$)가 전체 재발율에 영향을 끼치는 독립적인 인자로 확인되었다. 단기 성적 분석에서 점막하박리술-올가미병용절제술 군은 기존 점막하박리술 군에 비해 낮은 일괄 절제율(56.8% vs 96.5%, $p < 0.001$), 짧은 시술시간(45.6 vs 54.3 min, $P < 0.001$), 높은 천공 발생률(10.3% vs 6.0%, $p = .029$)을 보여주었다.

결론

점막하박리술-올가미병용절제술 군의 장기 예후는 기존 점막하박리술 군에 비해 좋지 않았다.

지만,다변량분석에서는병용절제술이전체재발률을포함한장기예후에영향을끼치는독립적인인자는아니었으며,일괄절제실패와종양의크기가장기예후에영향을끼치는독립적인위험인자였다.점막하박리술-올가미병용절제술의장기예후를향상시키기위한추가적노력이필요하다.