의학석사 학위논문

Novel Risk Stratification for the Recurrence after Endoscopic Resection of Advanced Colorectal Adenoma

진행성 대장 선종의 내시경적 절제술 후 재발의 위험도 분석에 대한 연구

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서 지 연

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Seoul National University

College of Medicine

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Novel Risk Stratification for the Recurrence after Endoscopic Resection of Advanced Colorectal Adenoma

by

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Abstract

Introduction: Advanced colorectal adenoma (ACA) is defined as colore ctal adenomas with at least one of three categories showing 1 cm or gr eater, villous component, and high-grade dysplasia. ACA has a high risk of developing colorectal cancer, and the recurrence rate is relatively hi gh after the endoscopic resection. The aims of this study were to asses s the clinical outcomes of ACA after endoscopic resection and identify risk factors of recurrence.

Methods: From January 2005 to December 2011, a total of 2,431 patients who underwent endoscopic resection for ACA in Seoul National University Hospital were retrospectively reviewed. Among them, 1,502 patients were excluded due to synchronous colorectal cancers, familial colorectal cancers, inflammatory bowel diseases, previous colorectal resection, and no follow-up colonoscopy. The primary outcomes were local recurrence and metachronous advanced neoplasm. Local recurrence was defined as detection of adenoma at the same site of previous resection. Metachronous advanced neoplasms were defined as detection of at least 1 ACA and/or adenocarcinoma at a follow-up colonoscopy.

Results: A total of 1,218 cases of ACA detected in 929 patients were enrolled. Median follow-up duration was 28.5 months (range, 12.8-51.7). Complete

resection was accomplished in 1,206 (99.0%) cases. Local recurrence and metachronous advanced neoplasm occurred in 45 (3.7%) and 170 (13.6%) cases, respectively. Cumulative rates of local recurrence in cases with 1 and 2-3 categories of ACA were 2.2% and 7.7% at 3 years, respectively. Cumulative rates of metachronous advanced neoplasm in cases with 3 or more adenomas were 18.6% and 22.5% at 3 years, respectively. Independent risk factors of local recurrence were ACA with 2 or 3 categories (hazard ratio [HR] 2.56, 95% confidence interval [CI] 1.36–4.81; p=0.004), laterally spreading tumor (HR 2.93, 95% CI 1.48–5.81; p=0.002), and piecemeal resection (HR 7.04, 95% CI 3.51–14.13; p<0.001). Independent risk factors of metachronous advanced neoplasm were male sex (HR 1.66, 95% CI 1.03–2.67; p=0.038), 3 or more adenomas (HR 2.52, 95% CI 1.70–3.74; p<0.001), and 3 or more of ACA (HR 1.43; 95% CI 1.01–2.04; p=0.049).

Conclusion: ACA with 2 or 3 categories could show higher local recurrence rate after the endoscopic resection than that in ACA with 1 category, which suggests the novel risk stratification of ACA according to the number of categories at index colonoscopy.

Keywords: advanced colorectal adenoma, endoscopic resection, recurrence

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ACA	advanced colorectal adenoma
CI	confidence interval
EMR	endoscopic mucosal resection
ESD	endoscopic submucosal dissection
HR	hazard ratio
IQR	interquartile range
LST	laterally-spreading tumor
MSTF	Multi-Society Task Force on Colorectal Cancer
mon	months
No	number
SNUH	Seoul National University Hospital
yr	years

Introduction

Colorectal cancer is the third most common cancer in men and the second in women worldwide[1]. The incidence rate is increasing rapidly in several areas especially in Asia, Eastern Europe, and South America, due to westernized diet and lifestyle[2]. However, both incidence rate and mortality rate are decreasing in United States[2]. These consequences probably originate from earlier detection with successful surveillance and improvement of treatment[3,4].

Colorectal cancer is typical cancer that follows adenoma-carcinoma sequence[5,6]. Adenoma, well known as precancerous lesion, becomes colorectal cancer in 5-15 years[5,7,8]. Advanced colorectal adenoma (ACA) is defined as adenoma with ≥10mm in size, villous histology, or high-grade dysplasia[9-11]. ACA has higher risk of adenocarcinoma, and recurrence rate is also high after the endoscopic resection[12-14]. Hence, risk stratification and appropriate surveillance is essential after the removal of ACA.

Guideline from the US Multi-Society Task Force on Colorectal Cancer (MSTF) recommended 3-year surveillance for each category of ACA: one or more tubular adenomas≥10mm, one or more villous adenomas, and adenoma with high-grade dysplasia[15]. Previous studies showed higher recurrence rate with adenomas larger than 10mm[9,16,17] and concluded 3-year follow-up would be adequate[14,18,19]. However, the other 2 conditions, villous histology and high-grade dysplasia, are supported by moderate quality of evidence. Besides, ACAs can be divided into two groups: those satisfying 1 category, and those

satisfying more than 2 categories of ACA. Comparisons of recurrence according to the number of categories were not ascertained yet. The aim of this study was to evaluate the outcome and clarify risk factors of recurrence in patients with ACA.

Materials and Methods

Study population

We retrospectively reviewed the medical records of 3,592 patients who underwent endoscopic resection for colorectal polyps from January 2005 to December 2011 in Seoul National University Hospital (SNUH). Among them, patients who had pathologic confirmation of ACA were enrolled in this study. The exclusion criteria were as follows: (i) patients with insufficient pathologic reports; (ii) patients with synchronous colorectal cancers; (iii) patients who had colorectal resection previously; (iv) patients with hereditary colorectal cancers like familial adenomatous polyposis or hereditary nonpolyposis colorectal cancer; (v) patients with inflammatory bowel diseases; (vi) patients who did not undergo follow-up colonoscopy.

Indications and techniques of polypectomy

Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) were performed for the resection of ACA. ESD was indicated for large (>20 mm in diameter) polyps that en bloc resection by snare EMR would be difficult[20]. Piecemeal resection was also performed for large polyps for which en bloc resection was technically difficult.

Injection-and-cut technique was used for EMR. After injection (NM-4U-1; Olympus, Japan) of diluted epinephrine with saline and indigocarmine,

circumferential lifting around polyp was checked. Adenoma was enclosed and grasped with snare wire (SD-12L/U-1; Olympus, Japan), cutting and coagulation of electrical current was applied for resection. In case of ESD, marking was performed around adenoma by a needle knife (KD-1L; Olympus, Japan) with electrical coagulation (20W, VIO 300D; ERBE, Tübingen, Germany). Solution of diluted epinephrine with saline and indigocarmine was injected surrounding adenoma. After lifted, mucosa was incised with needle knife and submucosa was dissected with IT knife. All procedures were performed by experienced endoscopists.

Follow-up colonoscopy and pathological review

After EMR or ESD, specimens were reviewed by expert pathologists. Considering endoscopic and pathologic findings, surveillance interval was decided by professional endoscopists. First follow-up was accomplished generally within 3 years according to the guidelines[15]. When patient had incomplete resection or piecemeal resection, follow-up was scheduled within 1 year. Additional colonoscopy was performed regardless of surveillance schedule when patients complained warning symptoms such as weight loss or gastrointestinal bleeding.

Measurement of outcomes

The primary outcome was recurrence after endoscopic resection for

ACA. Recurrence was classified into local recurrence and metachronous advanced neoplasm, which were not mutually exclusive. Local recurrence was defined as detection of adenoma at the same site of EMR or ESD. We reviewed interpretations of endoscopists and pictures of follow-up colonoscopy. Then whether recurrence occurred at the same site located on previous scar was confirmed. Metachronous advanced neoplasm was defined as newly detected advanced neoplasm at follow-up colonoscopy which was absent at index examination. We restricted ACA or adenocarcinoma as metachronous lesion, considering clinical significance.

The secondary outcomes were adverse events after endoscopic resection. Adverse events were classified into early bleeding, delayed bleeding, perforation, and post-polypectomy syndrome. Early and delayed bleeding were defined as bleeding within and over 24 hours after the endoscopic resection, respectively. Post-polypectomy syndrome was defined as syndrome that accompanied fever, abdominal pain and elevated leukocytes, which were consequences of serosal inflammation caused by thermal injury[21].

Definitions of risk variables

Age, sex, characteristics of adenoma, endoscopic procedure, pathologic reports were analyzed as risk factors. For location, we divided into the right side (cecum to transverse colon) and the left side of the colon (splenic flexure to rectum). Pathology of adenoma was categorized into tubular, tubulovillous,

and villous adenoma. Resection margin was grouped as positive, negative and could not be checked. The last category was adopted when margin of the specimen was unable to distinguish due to electrical ablation.

Additionally, number of categories for ACA was analyzed. For defining ACA, more than one condition should be fulfilled: adenoma with ≥10mm in size, villous histology, or high-grade dysplasia[22,23]. Satisfied numbers among these 3 conditions were counted and classified as 1 or ≥2. The number of adenomas, number of ACAs at index colonoscopy were also calculated, and classified as 1-2 or ≥3.

Statistical analysis

Values were expressed as the means ± standard deviations, median with interquartile range (IQR) or frequencies (percentages). Independent risk factors of local recurrence and metachronous advanced neoplasm were analyzed by Cox proportional hazards model. Variables associated with *P*-values under 0.05 in univariate analysis were included in multivariate analysis. Recurrence rates were calculated with actuarial life tables. Kaplan-Meier method was used to estimate the cumulative probabilities of local recurrence and metachronous advanced neoplasm. Log-rank test was performed to determine the significant differences in recurrence rates with respect to variables. In all analysis, *P*-value under 0.05 was considered to be statistically significant. All statistical analyses were performed with SPSS software (version 18.0; Chicago, IL, USA).

Results

Baseline characteristics

A total of 3,625 patients received colonoscopic polypectomy from January 2005 to December 2011 in SNUH. According to pathologic report, 120 had nonadenomatous polyps, 719 had adenomas which did not fulfill criteria of ACA, 2,431 had ACAs and 355 had colorectal cancers. Among 2,431 patients with ACAs, 1502 patients were excluded in line with exclusion criteria; 48 had insufficient pathologic reports, 638 accompanied colorectal cancers, 481 had colorectal resection previously, 16 had hereditary colorectal cancers, 33 had inflammatory bowel diseases, and 286 did not undergo follow-up colonoscopy. Finally, 1218 cases of ACAs detected in 929 patients were enrolled in this study.

Baseline characteristics of patients and ACAs are shown in Table 1. Mean age was 61.4 years (range, 27-85), male sex was predominant (*n*=678, 73.0%). Total number of the adenomas and ACAs per patient was 3.0±2.8 and 1.3±0.9, respectively, and mean size of the adenoma was 1.4±0.8cm. Majority of ACAs were located in the left side of the colon (*n*=749, 61.5%), and protruded type (*n*=1061, 87.1%). One hundred eighty-two adenomas (14.9%) were resected by the piecemeal method. Tubular adenoma (*n*=721, 59.2%), and low-grade dysplasia (*n*=943, 77.4%) were predominant in pathologic reports.

Table 1. Baseline characteristics of patients

Total number of patients	929
Total number of ACAs	1218
Age, years	61.4±9.1
Sex	
Male	678 (73.0 %)
Female	251 (27.0%)
Number of adenoma	3.0±2.8
Number of ACAs	1.3±0.9
Size, cm	
<1cm	157 (12.9%)
≥1cm	1061 (87.1%)
Site	
Right colon	469 (38.5%)
Left colon	749 (61.5%)
Type	
Protruded	1061 (87.1%)
Flat	43 (3.5%)
Laterally-spreading tumor	113 (9.3%)
Depressed	1 (0.1%)
Endoscopic resection	
EMR	1211 (99.4%)
ESD	7 (0.6%)
Type of resection	
En bloc	1036 (85.1%)
Piecemeal	182 (14.9%)
Complete resection (endoscopically)	
Yes	1206 (99.0%)
No	12 (1.0%)
Type of adenoma	
Tubular adenoma	721 (59.2%)
Tubulovillous adenoma	475 (39.0%)
Villous adenoma	22 (1.8%)
Dysplasia	
Low-grade dysplasia	943 (77.4%)
High-grade dysplasia	275 (22.6%)
Follow up duration (months)	28.5 (12.8–51.7)

Values are expressed as the mean±standard deviation, *n* (percentage) or interquartile range (IQR).

ACA, advanced colorectal adenoma; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection

Clinical outcomes of ACA after endoscopic resection

Clinical outcomes are shown in Table 2. Median follow-up duration was 28.5 months (IQR, 12.8-51.7), median time to first follow-up was 12.0 months (IQR, 11.0-17.0). Overall 1,206 (99.0%) ACAs had complete endoscopic resection. Twelve ACAs had incomplete resection initially, but only 5 of them had residual lesions at follow-up colonoscopy. Local recurrence occurred in 45 (3.7%), time to local recurrence was 12.7 months (IQR, 6.1–23.6). On the other hand, metachronous advanced neoplasms developed in 168 (13.8%): ACAs (*n*=153, 12.6%), and colorectal cancers (adenocarcinoma, *n*=15, 1.2%) were included. Median time to detection of metachronous lesion was 18.0 months (IQR, 12.1–39.7). Adverse events occurred after endoscopic resection of 40 (3.3%) adenomas. Among them, 16 (1.3%) lead to early bleeding and 12 (1.0%) delayed bleeding. Perforation was detected after endoscopic resection of 3 (0.2%) ACAs. Nine (0.7%) cases experienced post-polypectomy syndrome. There was no mortality case related to polypectomy.

Table 2. Clinical outcomes of the endoscopic resection

	n (%)
Local recurrence	45 (3.7%)
Metachronous advanced neoplasm	168 (13.8%)
Recurrence of ACA	153 (12.6%)
Recurrence of colorectal cancer	15 (1.2%)
Complication rate	40 (3.3%)
Early bleeding	16 (1.3%)
Delayed bleeding	12 (1.0%)
Perforation	3 (0.2%)
post-polypectomy syndrome	9 (0.7%)

ACA, advanced colorectal adenoma

Risk factors of local recurrence

Predictors of local recurrence and metachronous advanced neoplasm were analyzed separately. Results of univariate and multivariate analysis of local recurrence are displayed in Table 3. In univariate analysis, laterally-spreading tumor (LST, $P<0.001$), number of categories for ACA (≥2 categories; $P<0.001$), size of polyp ($P<0.001$), high-grade dysplasia ($P=0.002$), piecemeal resection ($P<0.001$), and positive resection margin ($P=0.001$) were significantly associated with local recurrence. Out of these factors, size and high-grade dysplasia were excluded for multivariable analysis due to the colinearity of factors. Multivariate analysis showed that LST (vs protruded type; HR, 2.93; 95% CI, 1.48–5.81; $P=0.002$), number of categories for ACA (≥2 vs 1 categories; HR, 2.56; 95% CI, 1.36–4.81; $P=0.004$), piecemeal resection (vs en bloc resection; HR, 7.04; 95% CI, 3.51–14.13; $P<0.001$) were independent risk factors of local recurrence. Differences of cumulative local recurrence rates according to the number of categories for ACA and type of resection are drawn in Figure 1 (log-rank test, $P<0.001$ for both). Additional subgroup analysis was performed for number of categories for ACA. Subgroups in each category, 1 or ≥2, had equal risks for local recurrence. In other words, adenomas≥10mm and ACAs with villous histology did not have significant difference for local recurrence. Adenomas ≥10mm with villous histology, ≥10mm with high-grade dysplasia and ACAs satisfying all 3 conditions showed higher risk than category 1, but had equal risks among

themselves. ACAs with only high-grade dysplasia (in category 1), with villous histology and high-grade dysplasia (in category ≥2) were not analyzed due to the absence of recurrence.

Table 3. Risk factors for local recurrence of ACA

Parameter	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age	1.03 (1.00–1.07)	0.088		
Sex (male/female)	0.74 (0.55–1.01)	0.055		
Type of polyp				
Protruded	1.00 (reference)			
LST	7.86 (4.30–13.38)	<0.001	2.93 (1.48–5.81)	0.002
Flat	0.92 (0.12–6.75)	0.932		
Depressed	0.00 (0.00–7.40)	0.980		
Site of polyp				
Right	0.89(0.49-1.62)	0.701		
Left	1.00 (reference)			
No of adenomas				
1-2	1.00 (reference)			
≥3	0.625 (0.34–1.14)	0.123		
No of ACAs				
1-2	1.00 (reference)			
≥3	0.48 (0.19–1.23)	0.125		
No of categories for ACA				
1	1.00 (reference)			
≥2	3.20 (1.72–5.96)	<0.001	2.56 (1.36–4.81)	0.004
Size of polyp	2.11 (1.74–2.57)	<0.001		
Pathology				
Tubular adenoma	1.00 (reference)			
Tubulovillous adenoma	1.50 (0.82–2.72)	0.186		
Villous adenoma	2.58 (0.61–10.97)	0.200		
High/low-grade dysplasia	2.57 (1.41–4.67)	0.002		
Type of resection				
Piecemeal/En bloc	11.44 (6.23–21.00)	<0.001	7.04 (3.51–14.13)	<0.001
Resection margin				
Negative	1.00 (reference)			
Positive	3.52 (1.69–7.31)	0.001		
Could not be checked	1.93 (0.97–3.82)	0.061		
Complete resection				
Incomplete/complete	2.60 (0.36–18.91)	0.345		

ACA, advanced colorectal adenoma; HR, hazard ratio; CI, confidence interval; LST, laterally-spreading tumor; No, number

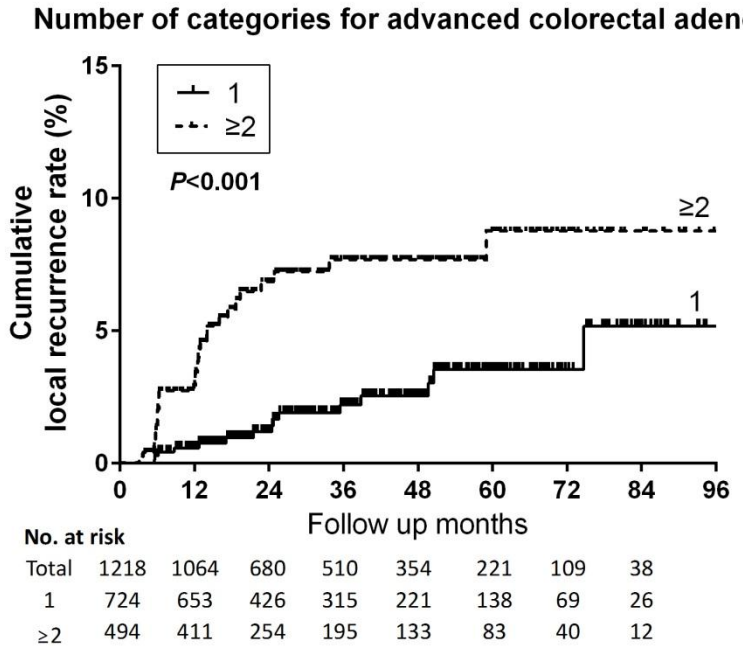

Figure 1. Cumulative probabilities of local recurrence rate according to number of categories for advanced colorectal adenoma (log-rank test, *P*<0.001)

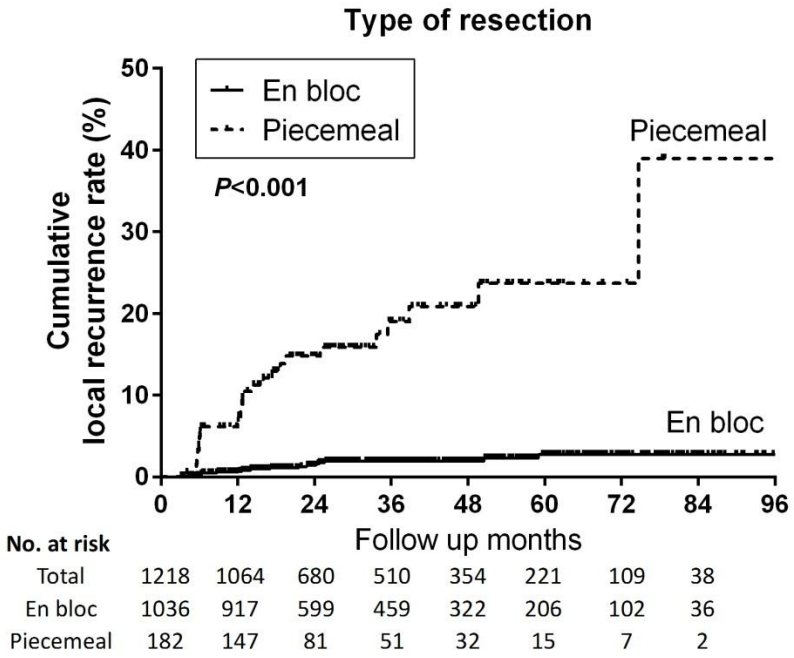

Figure 2. Cumulative probabilities of local recurrence rate according to type of resection (log-rank test, $P<0.001$)

Risk factors of metachronous advanced neoplasm

Next, risk factors of metachronous advanced neoplasm were analyzed with Cox-regression model (Table 4). Age (P=0.015), male sex (P<0.001), adenomas≥3 (P<0.001) and ACAs≥3 (P<0.001) were risk factors of metachronous lesions in univariate analysis. Multivariate analysis showed that male sex (vs female; HR, 1.66; 95% CI, 1.03–2.67; P=0.038), adenomas≥3 (vs 1 or 2 adenomas; HR, 2.52; 95% CI, 1.70–3.74; P<0.001), and ACAs≥3 (vs 1 or 2 ACAs; HR, 1.43; 95% CI, 1.01–2.04; P=0.049) were significantly related to metachronous lesions. Differences of cumulative rates of metachronous advanced neoplasm according to the number of adenomas and ACAs are drawn in figure 2 (log-rank test, P<0.001 for both).

Table 4. Risk factors for metachronous advanced neoplasms

Parameter	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age	1.02 (1.00–1.04)	0.015		
Sex (Male/Female)	2.30 (1.46–3.64)	0.000	1.66 (1.03–2.67)	0.038
Type of polyp				
Protruded	1.00 (reference)			
LST	0.64 (0.33–1.26)	0.197		
Flat	0.29 (0.07–1.15)	0.078		
Depressed	0.00 (0.00–1.52)	0.972		
Site of polyp				
Right	0.74(0.54-1.03)	0.072		
Left	1.00 (reference)			
No of adenomas				
1-2	1.00 (reference)			
≥3	3.16 (2.23–4.49)	0.000	2.52 (1.70–3.74)	0.000
No of ACAs				
1-2	1.00 (reference)			
≥3	2.39 (1.74–3.29)	0.000	1.43 (1.01–2.04)	0.049
No of categories for ACA				
1	1.00 (reference)			
≥2	0.76 (0.55–1.05)	0.097		
Size of polyp	1.06 (0.87–1.29)	0.596		
Pathology				
Tubular adenoma	1.00 (reference)			
Tubulovillous adenoma	1.08 (0.79–1.47)	0.642		
Villous adenoma	1.06 (0.39–2.88)	0.908		
High/low grade dysplasia	0.85 (0.57–1.26)	0.418		
Type of resection				
Piecemeal/En bloc	0.83 (0.50–1.37)	0.463		
Resection margin				
Negative	1.00 (reference)			
Positive	0.61 (0.35–1.07)	0.082		
Could not be checked	1.00 (0.71–1.41)	0.997		
Complete resection				
Incomplete/complete	0.59 (0.08–4.22)	0.603		

ACA, advanced colorectal adenoma; HR, hazard ratio; CI, confidence interval; LST, laterally-spreading tumor; No, number

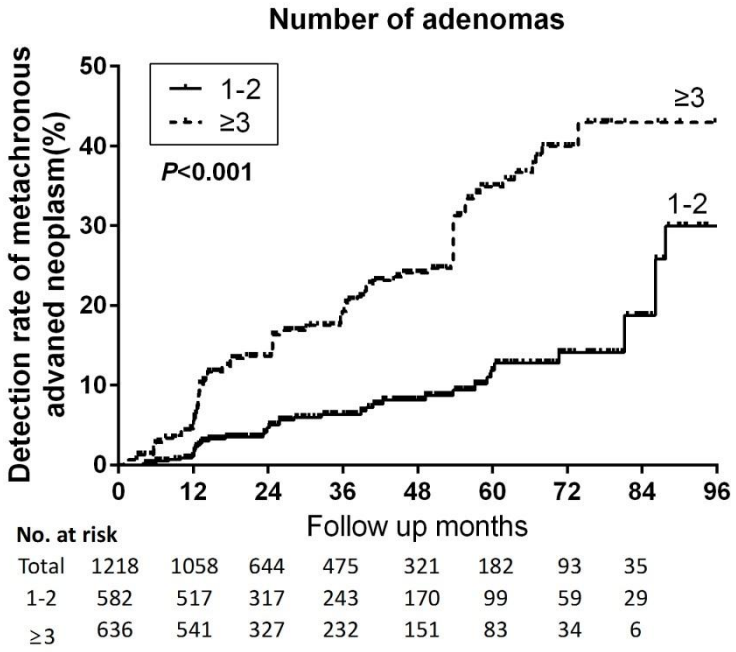

Figure 3. Cumulative probabilities of metachronous advanced neoplasm according to number of adenomas (log-rank test, $P<0.001$)

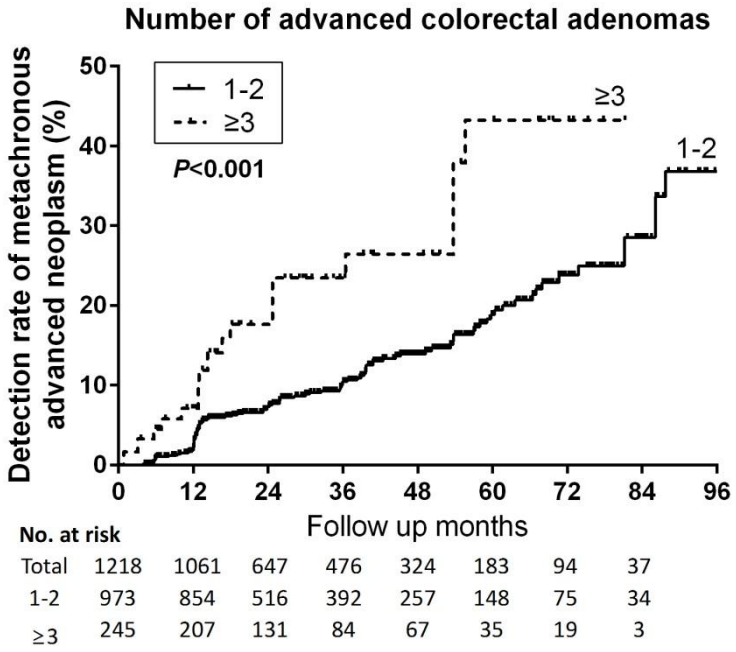

Figure 4. Cumulative probabilities of metachronous advanced neoplasm according to number of advanced colorectal adenomas (log-rank test, *P*<0.001)

Cumulative rates of local recurrence and metachronous advanced neoplasm

Cumulative rates of recurrence at 6 months, 1, 2, 3 and 5 years according to four risk factors were displayed in Table 5. For number of categories for ≥2 ACA, mean time to local recurrence was 13.3±11.2 months, and when piecemeal resection was performed, mean time to local recurrence was 17.1±16.2 months. When ≥3 adenomas or ACAs were accompanied, cumulative rates of metachronous advanced neoplasm were higher and recurrence occurred earlier than those in1 to 2 adenomas.

Table 5. Cumulative rates of recurrence and time to recurrence

Local recurrence							
No of categories for ACA	**6mon**	**1yr**	**2yr**	**3yr**	**5yr**	**Recur /total n (%)**	**Time to recurrence (mon)**
1	2 (0.3%)	4 (0.6%)	7 (1.2%)	11 (2.2%)	14 (3.5%)	15/724 (2.1%)	26.8±20.0
≥2	8 (1.9%)	14 (3.0%)	27 (6.8%)	29 (7.7%)	30 (8.8%)	30/494 (6.1%)	13.3±11.2
Type of resection							
En bloc	2 (0.2%)	6 (0.6%)	12 (1.4%)	15 (2.0%)	17 (2.8%)	17/1036 (1.6%)	18.9±15.5
Piecemeal	8 (5.0%)	12 (6.8%)	22 (14.8%)	25 (19.0%)	27 (23.7%)	28/182 (15.4%)	17.1±16.2
Metachronous advanced neoplasm							
No of adenomas	6mon	1yr	2yr	3yr	5yr	Recur /total n (%)	Time to recurrence (mon)
1-2	2 (0.5%)	6 (0.9%)	22 (4.5%)	27 (5.9%)	36 (10.8%)	44/582 (7.6%)	34.9±27.1
≥3	17 (1.8%)	28 (3.7%)	71 (12.9%)	90 (18.6%)	118 (33.3%)	124/636 (19.5%)	24.5±18.8
No of ACAs							
1-2	8 (0.6%)	17 (1.4%)	57 (6.8%)	72 (9.8%)	96 (17.1%)	110/973 (11.3%)	30.3±23.1
≥3	11 (3.3%)	17 (5.9%)	37 (16.6%)	45 (22.5%)	58 (42.5%)	58/245 (23.7%)	21.3±17.4

Values are expressed as the recurrence (cumulative recurrence rate, percentage), metachronous advanced neoplasm (cumulative detection rate, percentage) and mean±standard deviation.
ACA, advanced colorectal adenoma; No, number; mon, month; yr, year

Discussion

Summarizing this study elicited from 1218 ACAs, number of categories for ≥2 ACA, LST, and piecemeal resection were independent risk factors of local recurrence. LST[24,25] and piecemeal resection[24,26-28] are well known risk factors for local recurrence. Number of categories for ACA was a novel conception of risk stratification; significant difference of local recurrence between 1 category and ≥2 categories were demonstrated. High-grade dysplasia was not analyzed in subgroup due to insufficient number of recurrence. Frequency of high-grade dysplasia is quite low[16,29] so that it is difficult to get qualified data about high-grade dysplasia.

Meanwhile, male sex, ≥3 adenomas and ≥3 ACAs could predict metachronous advanced neoplasm. For metachronous lesions, number and size of adenomas[9,13,14,16-19], presence of villous histology[10,14,30] are known risk factors. In this study, we included only cases with ACAs at index colonoscopy. Therefore, yet it is similar with previous results, our result is novel finding. Owing to the differences of inclusion criteria, criteria of ACA such as size ≥10mm, villous histology, or high-grade dysplasia might have ruled out for significant risk factors.

Next, we analyzed recurrence rates and mean time to recurrence for each risk factor. Previous reports have demonstrated that detection rates of metachronous ACA after removal of ACA is recorded as 10% in 3 years[14] and 20-26% in 5 years[12,13]. Considering our follow-up duration, our data implied

similar rates. In cases with risk factors, time to metachronous advanced neoplasm was shorter and detection rates were higher.

Based on our results, we suggest shorter surveillance interval than previous guidelines for ACAs with risk factors. In other words, for ACAs satisfying 2 or 3 categories of ACA, combined with ≥3 adenomas and ≥3 ACAs, surveillance interval shorter than 3 years should be considered. Especially, short-term meticulous follow-up is required for ≥3 ACAs considering high recurrence rate.

For type of resection, MSTF mentioned that short interval colonoscopy (<1 year) is recommended when adenoma removed in piecemeal resection and completeness of resection is questionable[15]. Many studies already informed recurrence rate after piecemeal resection[24,25,27,28,31-35], however, data of cumulative recurrence along with time were limited. Reflecting our data, short interval of 1-year same as current guideline seems appropriate for piecemeal resection of ACA. Further investigation is necessary to determine adequate surveillance interval.

When interpreting our data, we should remind that median time to first follow-up in this study was 12.0 months (IQR, 11.0-17.0), which is quite shorter than previous guidelines. The medical cost for colonoscopy is remarkably low in Korea. Therefore, we tend to perform frequent colonoscopy and patients feel lower burden of charge than those in other countries. This specific circumstance enabled shorter surveillance than guidelines and it could support our claim of shorter interval than 3 years.

Our study has important advantages. This study contains all cases of ACAs during the study period. On the contrary, quite a few reports focused on specific part of ACA: restricted in size or type of polyps[21,26,27,36-40]. Therefore, our result could reflect generalized prognosis of ACA. Most outstanding substance is that we proposed novel conception of risk stratification. To the best of our knowledge, number of categories for ACA and number of ACAs are completely new concepts, because there has been no existing report comparing risk of recurrence according to each criteria of ACA. This result is vital for distinguishing ACA with higher risk of recurrence, which can be helpful for deciding surveillance interval after the resection of ACA.

There are several limitations of the study. First, this was retrospective cohort study. Second, designed in a single center, selection bias cannot be ignored. Particularly, since SNUH is a tertiary hospital, many patients were referred for defiant polyps. Third, quality of bowel preparation was not adjusted; number of adenomas or ACAs, and detection of recurrence might be influenced.

In conclusion, ACA with ≥2 categories showed higher local recurrence rate than that in ACA with 1 category, which suggests the novel risk stratification of ACA according to the number of categories at index colonoscopy.

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초 록

서론: 진행성 대장 선종은 대장 선종 중 크기가 1 cm 이상이거나 융모상 선종인 경우, 고도의 이형성이 동반된 경우를 말한다. 진행성 선종은 대장암 발생의 중요한 위험 인자이며 내시경적 절제술 후 재발률도 높은 편이다. 따라서 본 연구에서는 진행성 선종의 내시경적 절제술 후의 결과에 대해 정리하고 재발의 위험 인자에 대해 분석하고자 하였다.

방법: 2005년 1월부터 2011년 12월까지 서울대 병원에서 진행성 선종으로 대장내시경적 절제술을 시행한 2,431명의 환자를 검토하였다. 그 중, 1,502명은 동반된 대장암, 가족성 대장암, 염증성 대장염, 대장 절제술의 과거력, 추적 소실 등의 이유로 제외되었다. 본 연구에서 목표로 한 분석 결과는 국소 재발 및 이시성 재발이었다. 국소 재발은 내시경적 절제술을 시행한 동일 부위에 선종이 발견되는 것으로 정의하였고, 이시성 재발은 추적 관찰 시 1개 이상의 진행성 선종이나 선암이 발견된 경우로 정의하였다.

결과: 총 929명의 환자에서 발견된 1,218건의 진행성 선종에 대해 분석을 시행하였다. 추적 관찰의 중앙값은 28.5 (사분범위, 12.8–51.7) 개월이었고, 1,206 (99.0%) 진행성 선종에서 완전 절제가 확인되었다. 국소 재발과 이시성 재발은 각각 45 (3.7%), 170 (13.6%)에서 발생하였다. 진행성 선종의 조건 중 1가지를 만족하는 경우 3년 국소 누적 재발률이 2.2%, 2–3 가지를 만족하는 경우는 7.7%였다. 3개 이상의 선종이 있는 경우 3년 이시성 누적 재발률은 18.6%, 3개 이상의 진행성 선종이 있는 경우는 22.5%였다. 국소 재발의 위험 인자로는 진행성 선종의 조건 중 2–3개의 조건을 만족하는 경우 (위험도 2.56, 95% 신뢰구간 1.36–4.81; p=0.004), 측방 발육형 종양 (위험도 2.93, 95% 신뢰구간 1.48–5.81; p=0.002), 그리고 piecemeal 절제를 시행한 경우 (위험도 7.04, 95% 신뢰구간 3.51–14.13; p<0.001) 였다. 이시성 재발의 위험 인자로는 남성 (위험도 1.66, 95% 신뢰구간 1.03–2.67; p=0.038), 3개 이상의 선종을 동반한 경우 (위험도 2.52, 95% 신뢰구간 1.70–3.74; p<0.001), 또는 3개 이상의 진행성 선종을 동반한 경우 (위험도 1.43; 95% 신뢰구간 1.01–2.04; p=0.049) 였다.

결론: 진행성 선종의 조건 중 2–3개를 만족하는 경우는 1개를 만족하는 경우에 비해서 국소 재발이 유의하게 높았다. 이는

대장내시경 시행 후 진행성 선종이 발견되었을 때 만족하는 조건의 수에 따라서 위험도를 분석하는 새로운 방법으로 제시될 수 있다.

주요어: 진행성 대장 선종, 내시경적 절제, 재발
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