Risk of Metachronous Advanced Neoplasia in Patients With Multiple Diminutive Adenomas

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OBJECTIVES: **Individuals with advanced adenomas or three or more adenomas have a higher risk of metachronous advanced neoplasia (AN) and are recommended to undergo surveillance colonoscopy at shorter intervals. However, it is questionable whether patients with multiple (three or more) non-advanced diminutive adenomas should be considered as high-risk.**

METHODS: **We analyzed 5482 patients diagnosed with one or more adenomas during their first colonoscopy screening and who underwent a follow-up colonoscopy. Patients were categorized into four groups based on adenoma characteristics at baseline: Group 1, 1-2 non-advanced adenomas; Group 2, $\geq$3 non-advanced, diminutive (1 to 5 mm) adenomas; Group 3, $\geq$3 non-advanced, small (6–9 mm) adenomas; and Group 4, advanced adenomas.**

RESULTS: **During a median follow-up of 38 months, the incidence of metachronous AN at surveillance colonoscopy was 5.6%. The incidence of AN was 3.9% in group 1, 5.9% in group 2, 10.6% in group 3, and 22.1% in group 4. The adjusted hazard ratios (HRs) [95% confidence intervals (CIs)] for metachronous AN between group 2, group 3, and group 4, and low risk group 1 were 1.71 (0.99–2.94), 2.76 (1.72–4.44), and 5.23 (3.57–7.68), respectively. Compared with group 4, the adjusted HRs (95% CIs) for group 1, group 2, and group 3 were 0.19 (0.13–0.28), 0.32 (0.18–0.59), and 0.52 (0.31–0.89), respectively.**

CONCLUSIONS: **We found that patients with three or more non-advanced diminutive adenomas had a borderline increased risk of metachronous AN compared with patients with low risk adenomas.**

INTRODUCTION

Colorectal cancer (CRC) is worldwide the fourth most frequently diagnosed cancer worldwide and the second leading cause of overall cancer-related death [1]. The importance of early detection and removal of pre-cancerous lesions has been emphasized because the majority of CRC occur from pre-existing adenomatous polyps, after going through an adenoma-carcinoma sequence [2, 3]. The performance of polypectomy during colonoscopy can prevent CRC and reduce mortality. Early detection as well as advanced neoplasia (AN) surveillance after polypectomy are important to reduce CRC mortality, because patients with previous adenomas are at a higher risk of metachronous lesions [2–5]. Therefore, post-polypectomy surveillance has become a major indication for colonoscopy.

Guidelines recommend different follow-up surveillance colonoscopy intervals based on the number and characteristics of the detected adenomas during colonoscopy screening [6, 7]. Several high-risk factors are known to contribute to the development of AN, including the number of adenomas. As the number of adenomas increases, the risk of metachronous AN also increases. This trend is especially prevalent when there are three or more adenomas at index colonoscopy [8, 9]. In addition, any adenoma exhibiting high-risk traits is referred to as an advanced adenoma. High-risk traits include a size of 10 mm or more in diameter, and advanced histology of high-grade dysplasia or villous component. In patients with advanced adenomas, current guidelines recommend a short-term follow-up surveillance colonoscopy in three years, compared with 5–10 years for patients with 1 or 2 non-advanced adenomas [6, 9].

However, it is questionable whether patients with three or more adenomas without any other high-risk factors, especially when diminutive in size ($\leq$5 mm), should also be considered at a high

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risk of metachronous AN. In this study, we subclassified patients at high risk based on adenoma size (diminutive vs small) and the presence of advanced adenoma. We then assessed the risk of metachronous AN among different groups.

METHODS

Study setting and participants

We conducted a retrospective cohort study of healthy individuals aged 50 years and older who underwent first-time screening colonoscopy and subsequent surveillance colonoscopy at least 1 year apart between January 2006 and December 2017 at the Samsung Medical Center, South Korea ($n = 18,091$). We excluded 12,609 participants who met any of the following exclusion criteria: poor bowel preparation, incomplete colonoscopy, history of malignancy, history of colorectal surgery, inflammatory bowel disease, family history of colorectal CRC, no adenoma at screening, or sessile serrated adenoma/polyp or traditional serrated adenoma at screening. Finally, 5482 participants diagnosed with one or more colorectal adenomas at baseline and who underwent surveillance colonoscopy were included in this study (Fig. 1). The Institutional Review Board of the Samsung Medical Center approved this study and waived the requirement for informed consent because our data only consisted of de-identified data that had been collected with clinical purpose as part of the health screening check-up.

Measurement of variables

The comprehensive health-screening program included demographic characteristics, anthropometric measurements, endoscopy, and a self-administered health questionnaire on smoking status, alcohol intake, regular exercise, regular aspirin use, and family history of colon cancer. Weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, with the participants dressed in light clothing and bare feet. Body mass index (BMI) was calculated as weight in kilograms divided by height in square meters (kg/m²). Smoking status was categorized into three groups including never, former, and current smoker. Alcohol intake status was divided into mild ($\leq$10 g/day) and modest ($>$10 g/day).

Regular exercise was defined as exercising three or more times per week with moderate intensity.

Colonoscopies

Experienced board-certified gastroenterologists performed the colonoscopies after bowel preparation with polyethylene glycol solutions. A complete examination was defined as one that reached the cecum. Endoscopists assessed the location and size of the detected colorectal polyp. Location between cecum to splenic flexure was defined as proximal, and descending colon to rectum as distal. The size of each polyp was routinely estimated using open biopsy forceps. Endoscopists routinely resected the detected polyps during colonoscopy and the histopathology of biopsy samples were assessed by qualified pathologists. The following information was recorded in the electronic medical record after the colonoscopy: number of polyps, locations and sizes of polyps, the time and result of the last colonoscopy, family history of CRC, bowel preparation (Aronchick scale), and colonoscopy completeness.

Variables and definitions

The primary outcome of interest was the development of metachronous colorectal AN at follow-up colonoscopy. Advanced adenoma was defined as any adenoma 1-cm or more in size, or containing $\geq$25% of villous component or high-grade dysplasia. A diminutive adenoma was defined as an adenoma 1–5 mm in size, and a small adenoma was defined as an adenoma 6–9 mm in size. AN included advanced adenoma and invasive CRC. Baseline characteristics of participants including age, sex, BMI, smoking status, alcohol intake, regular exercise, regular aspirin use, and the adenoma detection rate (ADR) of the endoscopist were collected. ADR was used as a quality indicator of the colonoscopy. The ADR, determined by each endoscopist, was calculated from data of individuals $\geq$50-years-old who underwent a first-time screening colonoscopy, except cases with poor bowel preparation.

We categorized patients into four risk groups based on the number and characteristics of the colorectal neoplasms detected during colonoscopy screening: Group 1, low risk, one or two non-advanced adenomas; Group 2, three or more diminutive (1–5 mm) non-advanced adenomas; Group 3, three or more small (6–9 mm) non-advanced adenomas; and Group 4, high risk, advanced adenomas. The size was determined based on the largest adenoma.

Statistical analysis

Data were presented as mean ± standard deviation for continuous variables and percentages for categorical variables. The differences in baseline characteristics among the risk groups were compared using a one-way ANOVA test or a *t*-test for continuous variables and the χ^2 test for categorical variables. We performed univariable Cox regression analysis to identify whether an association existed between the baseline factors and the development of metachronous AN. The Kaplan–Meier method was used to describe the cumulative hazard of AN according to the risk groups. Further, we used multivariable Cox regression models to estimate adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for metachronous AN according to the risk groups. The multivariable
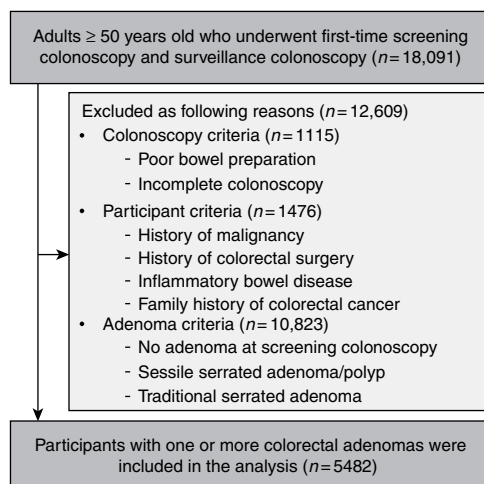


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┌─────────────────────────────────────────────────┐
│ Adults ≥ 50 years old who underwent first-time   │
│ screening colonoscopy and surveillance           │
│ colonoscopy (n = 18,091)                         │
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          │
          │      ┌──────────────────────────────────────────┐
          │      │ Excluded as following reasons (n = 12,609) │
          │      │ • Colonoscopy criteria (n = 1115)          │
          │      │   - Poor bowel preparation                 │
          │      │   - Incomplete colonoscopy                 │
          ├─────▶│ • Participant criteria (n = 1476)          │
          │      │   - History of malignancy                  │
          │      │   - History of colorectal surgery          │
          │      │   - Inflammatory bowel disease             │
          │      │   - Family history of colorectal cancer    │
          │      │ • Adenoma criteria (n = 10,823)            │
          │      │   - No adenoma at screening colonoscopy    │
          │      │   - Sessile serrated adenoma/polyp         │
          │      │   - Traditional serrated adenoma           │
          │      └──────────────────────────────────────────┘
          ▼
┌─────────────────────────────────────────────────┐
│ Participants with one or more colorectal adenomas │
│ were included in the analysis (n = 5482)          │
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Fig. 1 Flow chart of study participants

model was selected by backward stepwise selection method based on the Akaike information criterion (AIC). The candidate factors included baseline age, sex, BMI, smoking status, alcohol consumption, regular exercise, regular aspirin use, bowel preparation (excellent/good/fair), ADR of the endoscopist (screening), ADR of the endoscopist (surveillance), and year of screening examination. In the multivariable Cox regression analysis, we performed pairwise comparison of the risk for metachronous AN by considering risk groups 1, 2, and 4 as references. For these multiple comparisons, Bonferroni correction was used to adjust both P-value and the CIs of HR. A P-value of <0.05 was considered statistically significant. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) and R version 3.4.3 (The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Baseline characteristics ($n = 5482$) are presented in Table 1. The mean age (standard deviation) of participants was 55.5 (5.7) years; 68.5% were men. When stratified alongside the pre-defined risk groups, participants were categorized as follows: Group 1 ($n = 4302$), Group 2 ($n = 472$), Group 3 ($n = 378$), and Group 4 ($n = 330$). The low-risk group (Group 1) had a significantly higher ratio of young, women, less obese individuals, and non-smokers, as well as a longer surveillance interval, compared with the other groups. The number of baseline adenomas in groups with multiple adenomas of three or more, groups 2 and 3, showed a mean value of 3.7 and 4.0. In group 2, the proportion of the number of diminutive adenomas was 3 (61%), 4 (20.5%), 5 (11.9%), and 6–10

(6.6%), respectively. The majority of patients in groups 2 and 3 had 3–5 adenomas.

Table 2 presents the univariable and multivariable Cox regression analyses about baseline clinical factors associated with the development of metachronous AN. Among the patient factors, older age (adjusted HR, 1.04; 95% CI, 1.02–1.06) and male sex (adjusted HR, 1.80; 95% CI, 1.34–2.43) were significantly associated with the risk of metachronous AN. BMI was also a risk factor (unadjusted HR, 1.07; 95% CI 1.03–1.11), albeit being insignificant (adjusted HR, 1.03; 95% CI 0.99–1.08) in the multivariable analysis. ADR of the endoscopist was an independent predictor of metachronous AN. The risk of metachronous AN was decreased when screening was performed by an endoscopist with higher ADR (adjusted HR 0.97; 95% CI, 0.95–0.99). The ADR of the endoscopist who performed surveillance colonoscopy was also retained as an independent predictor of metachronous AN (adjusted HR, 1.04; 95% CI, 1.02–1.06).

During a median follow-up of 38 months, 309 AN developed in 5482 participants, with an incidence of 5.6%. The incidence of AN was 3.9% (168/4,302) in group 1, 5.9% (28/472) in group 2, 10.6% (40/378) in group 3, and 22.1% (73/330) in group 4 (Fig. 2). During the follow-up period, five interval CRCs were developed. In group 1, two (0.05%) interval ascending colon cancers were developed. In group 2, one (0.21%) interval rectal cancer was developed. In group 3, one (0.26%) interval sigmoid colon cancer was developed. In group 4, one (0.3%) interval ascending colon cancer was developed. Figure 3 shows the cumulative hazard for metachronous AN according to the risk groups. Group 4, including patients with advanced adenoma, had the highest hazard for AN devel-

Table 1 Baseline characteristics of risk groups based on adenoma characteristics at index colonoscopy

	Total ($N = 5482$)	Group 1 ($n = 4302$)	Group 2 ($n = 472$)	Group 3 ($n = 378$)	Group 4 ($n = 330$)	P value
Age (years)	55.5 ± 5.7	55.2 ± 5.6	56.7 ± 6.4	57.1 ± 6.1	56.9 ± 6.2	<0.001
Sex (%)						<0.001
Male	68.5	65.4	80.1	83.6	74.8	
Female	31.5	34.6	19.9	16.4	25.2	
Body mass index (kg/m²)	24.2 ± 2.8	24.1 ± 2.7	24.8 ± 2.8	24.6 ± 2.7	24.6 ± 2.7	<0.001
Smoking status (%)						<0.001
Never	44.8	47.4	36.2	30.4	39.0	
Past smoker	34.3	33.1	37.4	42.1	35.6	
Current smoker	20.9	19.4	26.5	27.5	25.4	
Alcohol intake (%)						0.12
Mild (≤10 g/day)	72.3	73.7	70.2	61.9	67.4	
Modest (>10 g/day)	27.7	26.3	29.8	38.1	32.6	
Regular exercise (%)	34.0	33.4	33.3	39.0	36.9	0.44
Regular aspirin use (%)	12.8	12.3	15.4	14.8	13.6	0.151
Surveillance interval (months)	38 (29–41)	38 (30–41)	33 (27–40)	33 (27–40)	36 (27–43)	<0.001
Number of adenoma at baseline	1.8 ± 1.4	1.3 ± 0.4	3.7 ± 1.2	4.0 ± 1.5	3.3 ± 2.7	<0.001

Values are expressed as means ± standard deviation, percentages, or median (interquartile range)

**Table 2** Risk of metachronous advanced neoplasia in univariable and multivariable analyses

	Univariable analysis		Multivariable analysis[a]	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Patient characteristics				
Age (years)	1.06 (1.04–1.08)	<0.001	1.04 (1.02–1.06)	<0.001
Male sex (%)	2.39 (1.78–3.20)	<0.001	1.80 (1.34–2.43)	<0.001
Body mass index (kg/m²)	1.07 (1.03–1.11)	<0.001	1.03 (0.99–1.08)	0.108
Current smoker (%)	1.84 (1.35–2.49)	<0.001		
Modest alcohol intake (%)	1.59 (1.25–2.02)	<0.001		
Regular exercise (%)	1.13 (0.89–1.43)	0.309		
Regular aspirin use (%)	1.65 (1.22–2.23)	0.001		
Colonoscopy quality indicators				
ADR of the endoscopist (screening)	0.98 (0.96–0.99)	0.019	0.97 (0.95–0.99)	0.004
Bowel preparation (Aronchick, %)				
Excellent	1.00 (reference)			
Good	0.95 (0.53–1.70)	0.871		
Fair	1.11 (0.60–2.04)	0.743		
ADR of the endoscopist (surveillance)	1.04 (1.02–1.06)	<0.001	1.04 (1.02–1.06)	<0.001
Baseline adenoma characteristics				
Low risk adenoma(s)	1.00 (reference)		1.00 (reference)	
Multiple diminutive adenomas	1.95 (1.14–3.34)	0.007	1.71 (0.99–2.94)	0.059
Multiple small adenomas	3.46 (2.18–5.51)	<0.001	2.76 (1.72–4.44)	<0.001
Advanced adenoma(s)	5.74 (3.34–8.33)	<0.001	5.23 (3.57–7.68)	<0.001

HR hazard ratio, *CI* confidence interval, *ADR* adenoma detection rate
[a]Multivariable model included above all variables and year of screening exam. The multivariable model selected by backward stepwise selection method based on Akaike information criterion (AIC)
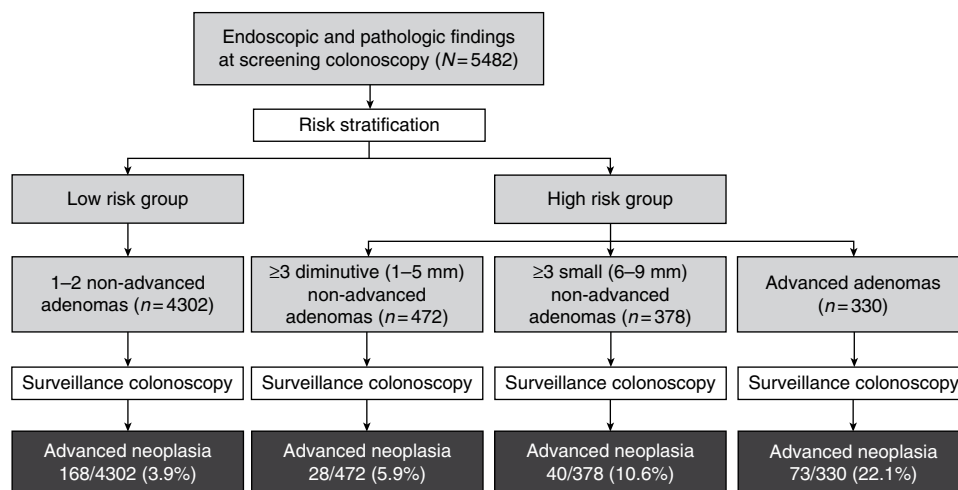
Fig. 2 Incidence of advanced neoplasia according to endoscopic and pathologic findings at screening colonoscopy

opment among the risk groups. In contrast, group 2, including patients with multiple diminutive adenomas, had a slightly higher hazard for AN than did the group 1, which had a low-risk. Table 3

presents the number of cases, incidence rate (95% CI), and the multivariable adjusted HR between the four prior categorized groups. Compared with group 1 (reference), adjusted HRs (95%
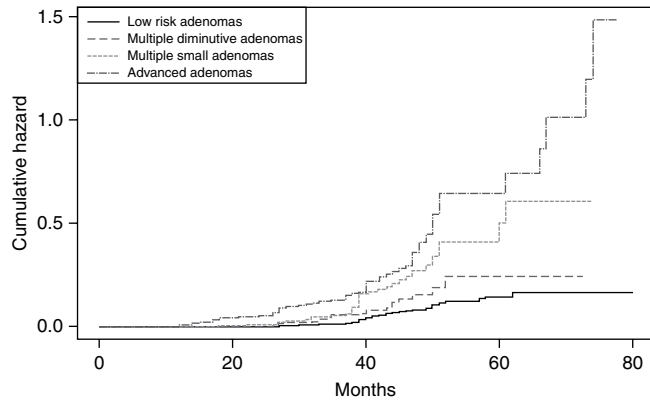
Fig. 3 Cumulative hazard of advanced neoplasia according to baseline adenoma characteristics

CIs) were increased across the risk groups, demonstrating 1.71 (0.99–2.94), 2.76 (1.72–4.44), 5.23 (3.57–7.68) for group 2, group 3, and group 4, respectively. This relationship was statistically significant for groups 3 and 4 ($P < 0.001$); by contrast, it was insignificant for group 2 ($P = 0.059$). Compared with group 4 (reference), adjusted HRs (95% CIs) for group 1, group 2, and group 3 were 0.19 (0.13-0.28), 0.32 (0.18-0.59), 0.52 (0.31-0.89), respectively. In addition, compared with group 2 (reference), adjusted HRs (95% CIs) for group 1, group 3, and group 4 were 0.59 (0.34–1.01), 1.62 (0.84–3.12), and 3.02 (1.65–5.51), respectively.

DISCUSSION

Current guidelines for surveillance colonoscopy in patients with high-risk factors recommend a short-term follow-up surveillance colonoscopy of 3 years after screening, compared with 5–10 years for patients with 1 or 2 non-advanced adenomas [10, 11]. Size ($\geq 10\,mm$), multiplicity (≥ 3), and presence of villous component or high-grade dysplasia are independent risk factors for metachronous AN [12, 13]. The risk of metachronous AN is higher in high-risk groups with any one of the factors mentioned above, but the contribution of each risk factor is less consistent [14, 15]. Indeed, we found that the risks of AN among individuals with high-risk features vary according to baseline adenoma characteristics. Among the high-risk group, patients with ≥ 3 diminutive (1–5 mm in size) adenomas, ≥ 3 small (6–9 mm in size) adenomas, and advanced adenomas developed AN at 5.9%, 10.6%, and 22.1%, respectively. In the multivariable analysis, patients with multiple diminutive adenomas had the lowest risk of AN among the subgroups with high-risk.

There remains some doubt that patients with ≥ 3 diminutive non-advanced adenomas really have an increased risk of AN at surveillance colonoscopy. The improvement of endoscopy image-enhancing technology has increased the detection rate of diminutive polyps. Indeed, ADRs of 40% or more have been reported in more recent studies [16]. Most previous studies have not subclassified sub-centimeter (<1 cm) adenomas into diminutive (1–5 mm) and small (6–9 mm) adenomas on screening colonoscopy [8, 15, 17]. In a recent study, researchers compared the risk of metachronous

AN in patients whose largest adenoma was diminutive (1–5 mm) versus small (6–9 mm) [18]. The study revealed that patients with diminutive adenomas had a low risk of metachronous AN regardless of the number of adenomas. Our study also demonstrated that patients with multiple diminutive adenomas had a low incidence (5.9%) of metachronous AN and had a borderline increased risk compared to patients with low risk adenomas.

In the diminutive group, the proportion of the number of diminutive adenomas was 3 (61%), 4 (20.5%), 5 (11.9%), and 6–10 (6.6%), respectively. The mean (standard deviation) number of adenomas was 3.7 ± 1.2 and most of them were distributed between 3 and 5. Because the sample size of 6–10 diminutive adenomas was so small, it is difficult to extend our results to 6–10 diminutive adenomas. Therefore, further studies assessing the risk of 6–10 diminutive adenomas are needed using adequate sample size.

Among adenoma characteristics, the two most known significant factors contributing to the higher risk of AN are the adenoma's size and multiplicity. Large adenomas (10 mm or more) contributed to more than a two-fold increase in the risk of AN, compared with sub-centimeter adenomas (<10 mm) [5, 9]. Size is certainly an important factor although this study did not show significant results in the subgroup analysis comparing diminutive and small adenomas. However, patients with ≥ 3 diminutive adenomas, with the largest sized 1–5 mm, had a significantly lower risk of metachronous AN than patients who had advanced adenomas at baseline.

In clinical practice, a majority of polyps detected and removed during screening colonoscopy are diminutive in size. More than 99% of diminutive adenomas are non-advanced in terms of histology, and the rate of invasive cancer is scarce [19–21]. Post-polypectomy surveillance guidelines should focus on patients with non-diminutive adenomas with high-risk factors (containing $\geq 25\%$ of villous component or high-grade dysplasia or $\geq 10\,mm$ in size, or ≥ 3 adenomas) and recommend short-term surveillance, because of the minimal risk associated with diminutive adenomas. Recent studies evaluating the time interval between screening and surveillance colonoscopy, have reported that the interval for low-risk patients has been lengthened [22–25]. The European Society of Gastrointestinal Endoscopy (ESGE) guidelines recommend repeating colonoscopy after 10 years from the index colonoscopy in low-risk patients with 1–2 small adenomas and low grade dysplasia. The surveillance interval for patients with multiple diminutive adenomas may be lengthened. Our findings suggest precise surveillance interval for patients with multiple diminutive non-advanced adenomas classified as intermediate risk from 3 to 5 years.

This study also provided important findings on colonoscopy quality. In the multivariable analysis, we considered the ADR of the endoscopists, which has been shown to predict the risk for interval caner after colonoscopy. The multivariable analysis indicated that the risk of metachronous AN was decreased when screening was performed by an endoscopist with a higher ADR. Our results underlined the importance of ADR as a prognostic factor for metachronous AN, to the same extent as patient- and adenoma-related factors at baseline. These data suggest that ADR,

COLON/SMALL BOWEL

Table 3 Risk for metachronous advanced neoplasia based on baseline adenoma characteristics (different reference groups)

	Total number	Number of cases	Incident rate (95% CI)	Multivariable-adjusted[a]					
				HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Group 1	4302	168	3.9 (3.3–4.5)	1.00 (reference)		0.19 (0.13–0.28)	<0.001	0.59 (0.34–1.01)	0.059
Group 2	472	28	5.9 (3.9–8.0)	1.71 (0.99–2.94)	0.059	0.32 (0.18–0.59)	<0.001	1.00 (reference)	
Group 3	378	40	10.6 (7.7–13.5)	2.76 (1.72–4.44)	<0.001	0.52 (0.31–0.89)	0.008	1.62 (0.84–3.12)	0.309
Group 4	330	73	22.1 (18.2–26.1)	5.23 (3.57–7.68)	<0.001	1.00 (reference)		3.07 (1.69–5.56)	<0.001

HR hazard ratio, *CI* confidence interval
[a]Multivariable model adjusted for baseline age, sex, body mass index, ADR of the endoscopist (screening), ADR of the endoscopist (surveillance), and year of screening exam, which were selected by backward stepwise selection method

possibly in combination with patient-related factors other than just colonoscopy findings, could be used to design cost-effective colonoscopic surveillance intervals [26].

Several limitations should be considered when interpreting our findings. First, misclassification may have occurred when the size of the polyp was roughly measured with an open biopsy as a reference. However, because endoscopists and pathologists were unaware of the study objectives, these measurement errors would be non-differential and could possibly result in an underestimation of the association between adenoma characteristics and metachronous colorectal AN. Second, our study was a single-center, retrospective study and included asymptomatic Korean men and women; therefore, it may be difficult to generalize our findings to other populations. Third, in this study, the median interval of surveillance was shorter than the intervals recommended in the current guidelines, especially in low-risk patients. Surveillance colonoscopy was recommended at 5–10 years in US at 5 years in Korean guidelines [6, 7] among low-risk individuals. Early examination could have reduced the incidence of AN; thus, the incidence rate of AN may have been underestimated in these patients. Therefore, it is unclear whether there is a substantial difference in the risk of metachronous AN related to differences in surveillance intervals.

This study also has considerable strengths, including its cohort design, relatively large sample size, the inclusion of first-time screening colonoscopies, and consideration of colonoscopy-quality indicators, such as ADR of the endoscopists, bowel preparation and incompleteness of colonoscopy.

In conclusion, substantial variation in the risk of metachronous AN exists among patients with high-risk factors based on adenoma characteristics such as size and advanced features. Among the high-risk group, patients with advanced adenomas had the highest risk of metachronous AN, followed by those with ≥3 small adenomas, and those with ≥3 diminutive adenomas. Because patients with multiple diminutive adenomas have the lowest risk of metachronous AN among the high-risk groups and they had a borderline increased risk compared to patients with low-risk adenomas, the optimal surveillance interval for these patients may be lengthened to reflect differences in risk. Further studies are needed

to verify our findings, because optimizing surveillance interval reduce underuse and overuse of surveillance colonoscopy, thus having substantial economic implications.

Study Highlights

WHAT IS CURRENT KNOWLEDGE
✓ Patients with advanced adenomas or ≥3 adenomas have a higher risk of advanced neoplasia (AN) or colorectal cancer and are recommended to undergo surveillance colonoscopy in 3 years after polypectomy.
✓ However, it is questionable whether patients with only multiple (three or more) non-advanced diminutive adenomas should be considered as high-risk.

WHAT IS NEW HERE
✓ Risks for AN among individuals with high-risk features vary based on baseline adenoma characteristics.
✓ We found that patients with three or more non-advanced diminutive adenomas had a borderline increased risk of metachronous AN compared with patients with low risk adenomas.
✓ The surveillance interval for patients with multiple diminutive adenomas may be lengthened from the recommended 3-year interval that is used for high-risk patients.

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