



Dynamic adenoma detection rate influences the risk of metachronous advanced neoplasia after removal of low-risk findings in screening colonoscopy

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Abstract

Background Endoscopists' adenoma detection rate (ADR) may change over time and dynamic ADR has been identified as a predictor for post-screening colorectal cancer. However, whether low-risk findings removed by an endoscopist with a lower dynamic ADR benefit from a shorter duration of follow-up requires further research.

Methods We conducted a two-center retrospective study of individuals who had low-risk findings removed and underwent subsequent surveillance colonoscopy. Endoscopists' dynamic ADR was the ADR of the previous 100 screening colonoscopies performed by the same endoscopist. A Cox-regression model and Kaplan–Meier survival analysis were used to explore the relationship between dynamic ADR and metachronous advanced colorectal neoplasia (ACRN).

Results Totally, 3471 individuals who had low-risk findings removed in baseline colonoscopy were included in analysis. Decreasing endoscopists' dynamic ADR was independently associated with metachronous ACRN. A 3.97-, 2.21-, and 2.67-fold increased risk for metachronous ACRN was observed in individuals of which baseline colonoscopy was performed by an endoscopist with a dynamic ADR of < 15%, 15–19%, and 20–24%, respectively, compared with those with the highest dynamic ADR (≥ 25%). The cumulative incidence of metachronous ACRN reached the 5% threshold at 4.5 years, 7.3 years, and 6.2 years in the dynamic ADR < 15%, 15–19%, and 20–24% group, respectively.

Conclusion Endoscopists' dynamic ADR influences the risk of metachronous ACRN after removal of low-risk findings in screening colonoscopy. Individuals undergoing removal of low-risk findings in screening colonoscopy by an endoscopist with a dynamic ADR < 25% may benefit from a shorter duration of follow-up interval.

Keywords Colonoscopy · Surveillance interval · Dynamic adenoma detection rate · Advanced colorectal neoplasia

Colorectal cancer (CRC) is the second most common cause of cancer-related deaths worldwide [1]. Colonoscopy is a commonly used procedure for CRC screening, which reduces CRC incidence and mortality by removing precancerous lesions and detecting early-stage CRC. To further lower the risk of metachronous CRC, individuals are advised

to undergo surveillance colonoscopy after polypectomy based on the pathology of polyps [2, 3].

The most recent 2020 US Multi-Society Task Force guideline recommended a 5–10 years surveillance interval for individuals who had low-risk findings (1–2 low-risk adenomas or 1–2 low-risk sessile-serrated lesions) in screening colonoscopy [2]. Previous research has focused on the risk factors for metachronous advanced colorectal neoplasia (ACRN) in individuals who had low-risk finding in screening colonoscopy [4–8], as well as on the development of models for risk stratification and optimization of the surveillance strategy [9]. However, the results from these studies varied, and the majority of them focused on the association of clinical characteristics and colonoscopic findings with metachronous ACRN rather than on the competency of endoscopist performing the screening colonoscopy. The relationship between competency of endoscopist performing the

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examination and the risk of metachronous ACRN requires further investigation.

The adenoma detection rate (ADR) of the endoscopist performing the baseline colonoscopy has been found to be inversely associated with the risk of incident and fatal CRC after negative colonoscopy and polypectomy [10]. A study has developed a clinical prediction model including clinical characteristics and endoscopists' ADR for risk stratification and surveillance strategy after polypectomy, which demonstrated moderate predictive value [11]. Nevertheless, earlier studies defined ADR over all colonoscopies performed annually or within the study period, which cannot account for a possible learning effect of endoscopist and reflect the short-term competency of endoscopist. Thus, a novel, dynamical calculation of ADR was first used in a nation-wide retrospective study and was found to be a predictor for post-screening CRC after negative colonoscopy and polypectomy [12]. However, whether low-risk findings removed by an endoscopist with a lower dynamic ADR benefit from a shorter duration of follow-up requires further research.

The aim of this study was to determine the relationship between endoscopists' dynamic ADR and other clinical characteristics in individuals with low-risk findings in screening colonoscopy and the risk of metachronous ACRN, and to provide optimal surveillance interval recommendation based on the cumulative incidence of metachronous ACRN.

Materials and methods

Study population

All first-time screening colonoscopy data were retrospectively collected from endoscopic procedure database at Huadong hospital (From August, 2012 to August, 2023) and Tongji Hospital (From January, 2012 to June, 2019) in Shanghai, China. Patient age and gender, bowel preparation, and endoscopic manifestation were all documented. Polyp characteristics such as location and size were extracted from endoscopic reports, and the histological information of polyps was obtained from another electronic database in these two hospitals.

Figure 1 shows the flowchart of study participant selection. All patients who underwent a first-time colonoscopy, had low-risk finding detected, and underwent at least one surveillance colonoscopy, were included in the analysis. Low-risk findings were defined as having any of the following: 1–2 tubular adenomas < 10 mm in size or 1–2 SSLs < 10 mm in size.

In order to ensure the quality of baseline colonoscopy and reduce the bias from missed diagnosis, the baseline colonoscopies having poor bowel preparation (Boston Bowel Preparation Scale < 6 score) were excluded. In order to ensure the quality of surveillance colonoscopy,

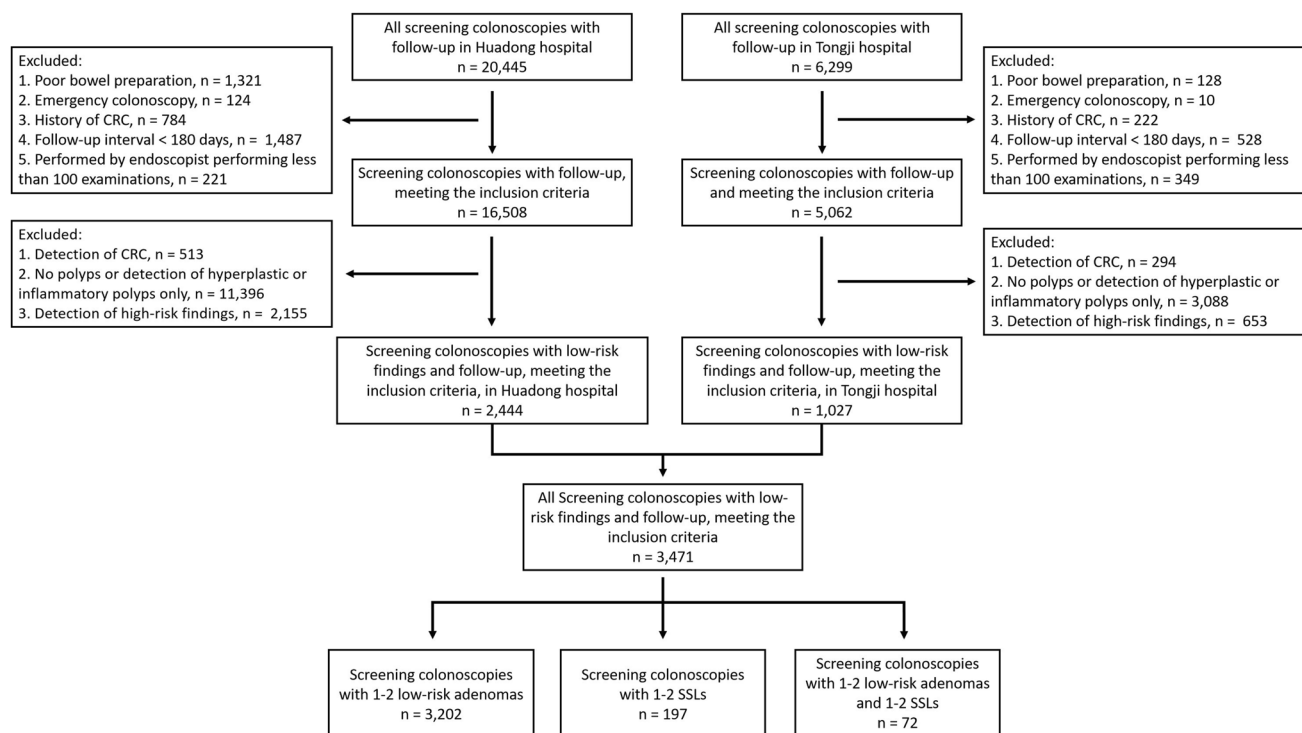


Fig. 1 Study flow diagram

follow-up discontinued when the surveillance colonoscopy met one of the following conditions: (1) presence of ACRN, (2) poor bowel preparation, and (3) performed by an endoscopist with a low ADR (< 15%). Findings from surveillance colonoscopies within half a year of the baseline were considered as synchronous findings and missed diagnosis of baseline colonoscopy. Thus, patients with a follow-up interval less than six months were also excluded.

The Huadong Hospital Ethics Committee approved this study. This study was a retrospective and observational study, and patient consent is not signed by each patient.

Patient-level factors

In this study, we considered a range of candidate predictors for metachronous ACRN, including patient age at baseline, gender, and polyp characteristics based on number, maximum size, and location at baseline colonoscopy. All detected polyps were removed by biopsy forceps, cold snare polypectomy, hot snare polypectomy, or endoscopic mucosal resection, determined by the endoscopists' choice. The size of polyps was estimated by visual assessment. The proximal colon was defined as the cecum, ascending colon, hepatic flexure, transverse colon, and splenic flexure, while the distal colon was defined as the descending colon, sigmoid colon, and rectum.

Endoscopist-level factors

In this study, we considered a novel, dynamic calculation of ADR as predictor for metachronous ACRN. The dynamic ADR was recomputed each time an endoscopist performed a colonoscopy as the proportion of colonoscopies with at least one adenoma detected in the previous 100 screening colonoscopies performed by this endoscopist. The first 99 examinations of each endoscopist, or examinations from endoscopist who performed fewer than 100 examinations, were excluded from further analysis.

Study outcome

The primary outcome measure was metachronous ACRN. ACRN was defined as CRC or advanced adenoma that presented one of the following features: a tubulovillous or villous component, high-grade dysplasia, or ≥ 10 mm diameter.

Sensitivity analysis

In our study, we conducted two sensitivity analysis. Patients who underwent several surveillance colonoscopies and had low-risk adenomas/SSLs removed during follow-up were also included, which may delay the time point of

metachronous ACRN detection in these patients. Thus, a first sensitivity analysis was performed in a subset of patients who did not have low-risk adenomas/SSLs removed during follow-up. In addition, we considered that calculating dynamic ADR based on 100 previous colonoscopies may result in rapid fluctuations in dynamic ADR and a less reliable estimate. Therefore, a second sensitivity analysis was performed by calculating the dynamic ADR based on previous 200 colonoscopies, which led to a better estimate, and exploring the association between dynamic ADR and metachronous ACRN.

Statistical analysis

Descriptive statistics were used to describe clinical characteristics of baseline colonoscopy. The Categorical variables were presented as numbers and frequencies, and continuous variables with normal and non-normal distribution were presented as mean (standard deviation (SD)) or median (interquartile range (IQR)), respectively.

The relationship between dynamic ADR of endoscopist performing the baseline colonoscopy and metachronous ACRN was determined using multivariate Cox-regression models when adjusting for confounding factors, including patient age, gender, number, maximum size, and location of adenomas/SSLs at baseline colonoscopy. Kaplan–Meier survival analysis were plotted for cumulative incidence of metachronous ACRN in subsets of patients stratified by dynamic ADR. The time point when the cumulative incidence of metachronous ACRN during follow-up reached the 5% threshold, was an important indicator for optimal surveillance interval. The 5% threshold was based on a previous meta-analysis study that reported that the pooled 5-year cumulative incidence of advanced adenomas was 4.9% for individuals who had low-risk adenomas [13].

Two-sided P-values < 0.05 were considered significant. All analysis were performed using R (R foundation for Statistical Computing, Vienna, Austria).

Results

Participants and baseline characteristics

As shown in Fig. 1, 16,508 first-time screening colonoscopies at Huadong hospital and 5062 first-time screening colonoscopies at Tongji hospital met the inclusion criteria and had subsequent surveillance colonoscopies. Among these, 3471 patients (2444 patients at Huadong hospital and 1027 patients at Tongji hospital) with low-risk findings at baseline colonoscopy were included in the analysis.

For the entire study cohort, 57.5% were male, and the median age was 59 (IQR, 52–65). 94.3% and 7.7% of patients had at least one low-risk adenoma and low-risk SSL at baseline colonoscopy, respectively. 2.1% of patients had both low-risk adenomas and low-risk SSLs at baseline colonoscopy. The proportion of patients whose baseline colonoscopy was performed by an endoscopist with a dynamic ADR of < 15%, 15–19%, 20–24%, and $\geq 25\%$ was 11.2%, 28.8%, 32.1%, and 28.0%, respectively. The median follow-up time obtained by a reverse Kaplan–Meier method was 2.34 years (Table 1).

To illustrate the changes in dynamic ADR over time for endoscopists in the two hospitals, the variation in the endoscopist with the highest average dynamic ADR, the endoscopist with the lowest average dynamic ADR, and the overall average dynamic ADR for all endoscopists with increasing case numbers were presented in Fig. 1S. As shown in Fig. 1S, the overall average dynamic ADR for all endoscopists in Tongji Hospital gradually increased to over 20% with increasing case numbers and remained above that level. Similarly, the overall average dynamic ADR for all endoscopists in Huadong Hospital also increased with case number but stayed below 20%.

Risk factors for metachronous ACRN

As shown in Table 2, a multivariate Cox-regression model revealed a significant association of metachronous ACRN with patient age at baseline colonoscopy (Aged 50–59, HR (95% CI), 11.3(1.51–84.6), $p=0.018$; Aged 60–69, HR (95% CI), 15.4(2.08–113), $p=0.007$; Aged ≥ 70 , HR (95% CI), 28.5(3.76–216), $p=0.001$, compared with aged < 50) and with the dynamic ADR of endoscopist performing the baseline colonoscopy (Dynamic ADR 0.2–0.24, HR (95% CI), 2.67(1.08–6.60), $p=0.033$; Dynamic ADR 0.15–0.19, HR (95% CI), 2.21(0.87–5.60), $p=0.093$; Dynamic ADR < 0.15, HR (95% CI), 3.97(1.52–10.3), $p=0.005$, compared with dynamic ADR ≥ 0.25). There was no significant relationship between metachronous ACRN and the number, location, or maximum size of low-risk adenomas and low-risk SSLs (All $p>0.05$).

The cumulative incidence of metachronous ACRN in subsets stratified by patient age and dynamic ADR

When stratified by patient age at baseline colonoscopy, the cumulative incidence of metachronous ACRN reached 5% threshold at 7.3 years, 6.3 years, and 3.7 years in patients aged 50–59, aged 60–69, and aged ≥ 70 , respectively. The cumulative incidence of metachronous ACRN never reached 5% threshold in patients aged < 50 (Fig. 2A).

When stratified by the dynamic ADR of endoscopist performing the baseline colonoscopy, the cumulative incidence of metachronous ACRN reached 5% threshold at 4.5 years, 7.3 years, and 6.2 years in patients whose baseline colonoscopy was performed by an endoscopist with a dynamic ADR of < 15%, 15–19%, and 20–24%, respectively. The cumulative incidence of metachronous ACRN never reached the 5% threshold in patients whose baseline colonoscopy was performed by an endoscopist with a dynamic ADR $\geq 25\%$ (Fig. 2B).

Sensitivity analysis

In the first sensitivity analysis, in which patients who had low-risk adenomas/SSLs removed during follow-up were excluded, the similar results were observed that the dynamic ADR of endoscopist performing the baseline colonoscopy was an independent predictor for metachronous ACRN (Dynamic ADR 0.2–0.24, HR (95% CI), 3.24(1.22–8.60), $p=0.018$; Dynamic ADR 0.15–0.19, HR (95% CI), 2.84(1.05–7.68), $p=0.04$; Dynamic ADR < 0.15, HR (95% CI), 4.37(1.53–12.5), $p=0.006$, compared with dynamic ADR ≥ 0.25) (Table 3). The cumulative incidence of metachronous ACRN reached the 5% threshold at 4.5 years, 6.5 years, and 5.2 years in individuals whose baseline colonoscopy was performed by an endoscopist with dynamic ADR of < 15%, 15–19%, and 20–24%, respectively (Fig. 3A).

In the second sensitivity analysis, when the dynamic ADR was calculated based on previous 200 colonoscopies, the similar results were observed that the dynamic ADR of the endoscopist who performed the baseline colonoscopy was an independent predictor of metachronous ACRN (Dynamic ADR 0.2–0.24, HR (95% CI), 11.4(1.53–84.5), $p=0.017$; Dynamic ADR 0.15–0.19, HR (95% CI), 11.5(1.54–85.3), $p=0.017$; Dynamic ADR < 0.15, HR (95% CI), 17.0(2.23–130), $p=0.006$, compared with dynamic ADR ≥ 0.25) (Table 4). Furthermore, the cumulative incidence of metachronous ACRN reached the 5% threshold at 4.6 years, and 6.2 years in individuals of which baseline colonoscopy was performed by an endoscopist with dynamic ADR of < 15% and 20–24%, respectively (Fig. 3B).

Discussion

The 2020 US Multi-Society Task Force guideline recommended a follow-up interval of 5 to 10 years for individuals who had low-risk findings completely removed in screening colonoscopy [2]. However, this follow-up recommendation did not take into account individuals' clinical characteristics and the quality of baseline colonoscopy, both of which may influence the risk of metachronous ACRN. Furthermore,

Table 1 Characteristics of patients enrolled

	Overall data (<i>n</i> = 3471)	Tongji hospital (<i>n</i> = 1027)	Huadong hospital (<i>n</i> = 2444)
Patients' factors			
Age at first colonoscopy (n(%))			
< 50 years	662 (19.1)	145 (14.1)	517 (21.2)
50–59 years	1074 (30.9)	295 (28.7)	779 (31.9)
60–69 years	1294 (37.3)	446 (43.4)	848 (34.7)
≥ 70 years	441 (12.7)	141 (13.7)	300 (12.3)
Male gender (n(%))	1996 (57.5)	594 (57.8)	1402 (57.4)
Endoscopic findings			
Number of adenomas (n(%))			
0	197 (5.7)	50 (4.9)	147 (6.0)
1	2426 (69.9)	759 (73.9)	1667 (68.2)
2	848 (24.4)	218 (21.2)	630 (25.8)
location of adenomas (n(%))			
None	197 (5.7)	50 (4.9)	147 (6.0)
Distal colon	1442 (41.5)	427 (41.6)	1015 (41.5)
Proximal colon	1626 (46.8)	516 (50.2)	1110 (45.4)
Distal and Proximal Colon	206 (5.9)	34 (3.3)	172 (7.0)
Maximum size of adenomas (n(%))			
None	197 (5.7)	50 (4.9)	147 (6.0)
≤ 5 mm	1639 (47.2)	400 (38.9)	1239 (50.7)
6–9 mm	1635 (47.1)	577 (56.2)	1058 (43.3)
Number of SSLs (n(%))			
0	3202 (92.3)	959 (93.4)	2243 (91.8)
1	224 (6.5)	67 (6.5)	157 (6.4)
2	45 (1.3)	1 (0.1)	44 (1.8)
location of SSLs (n(%))			
None	3202 (92.3)	959 (93.4)	2243 (91.8)
Distal colon	154 (4.4)	40 (3.9)	114 (4.7)
Proximal colon	108 (3.1)	28 (2.7)	80 (3.3)
Distal and Proximal Colon	7 (0.2)	0 (0.0)	7 (0.3)
Maximum size of SSLs (n(%))			
None	3202 (92.3)	959 (93.4)	2243 (91.8)
≤ 5 mm	155 (4.5)	32 (3.1)	123 (5.0)
6–9 mm	114 (3.3)	36 (3.5)	78 (3.2)
Endoscopists' factor			
dynamic ADR (n(%))			
≥ 0.25	972 (28.0)	323 (31.5)	649 (26.6)
0.20–0.24	1111 (32.0)	341 (33.2)	770 (31.5)
0.15–0.19	999 (28.8)	275 (26.8)	724 (29.6)
< 0.15	389 (11.2)	88 (8.6)	301 (12.3)
Median Follow-up Time (95% CI)	2.34(2.25–2.44)	1.80(1.69–1.88)	2.71(2.61–2.81)

ADR Adenoma detection rate, SSL Sessile serrated lesion, CI Confidence interval

the guideline provided a range of surveillance interval recommendation, which challenged endoscopists in deciding whether to recommend a 5-year follow-up, a 10-year follow-up, or a more ambiguous 5 to 10-year window. These

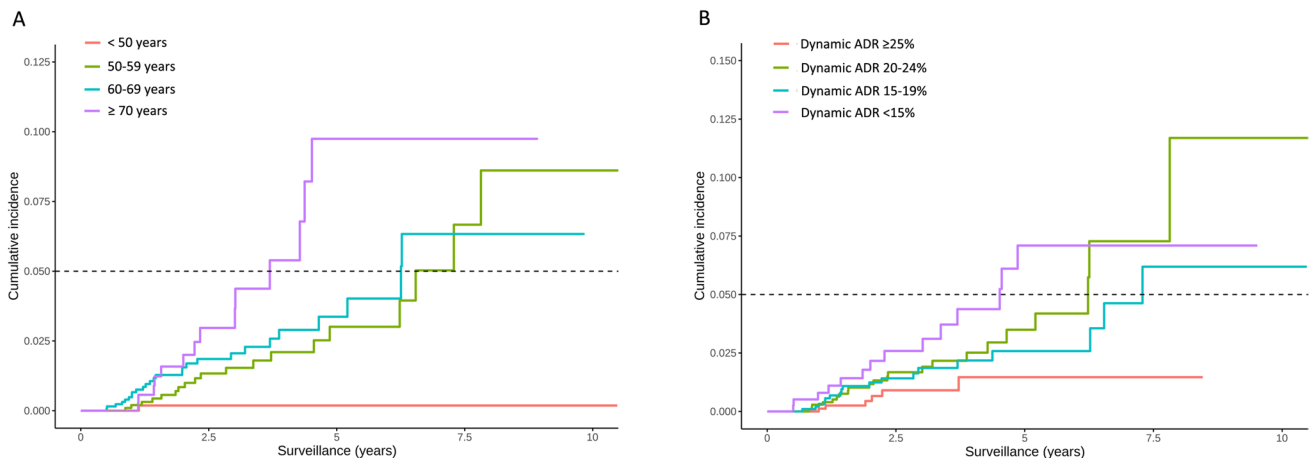
limitations reduce the clinical practicality and increase the risk of post-screening CRC.

The low-quality of baseline colonoscopy was one of the potential risk factors for metachronous ACRN, due to the missed diagnosis of high-risk findings or underestimation of

Table 2 Results of cox-regression model using metachronous advanced neoplasia as the outcome measure

	Univariate		Multivariate	
	HR (95% CI)	<i>p</i> value	HR (95% CI)	<i>p</i> value
Age				
< 50 years	Reference		Reference	
50–59 years	11.1(1.49–83.0)	0.019	11.3(1.51–84.6)	0.018
60–69 years	15.0(2.03–111)	0.008	15.4(2.08–113)	0.007
≥ 70 years	28.0(3.69–212)	0.001	28.5(3.76–216)	0.001
Male gender	1.10(0.66–1.84)	0.710		
Dynamic ADR				
≥ 0.25	Reference		Reference	
0.20–0.24	2.61(1.06–6.45)	0.037	2.67(1.08–6.60)	0.033
0.15–0.19	2.07(0.82–5.24)	0.125	2.21(0.87–5.60)	0.093
< 0.15	3.79(1.45–9.87)	0.006	3.97(1.52–10.3)	0.005
Characteristics of adenomas				
Number of adenomas	1.43(0.89–2.31)	0.138		
Location of adenomas				
Presence of proximal adenomas	1.50(0.89–2.51)	0.124		
Presence of distal adenomas	0.70(0.42–1.16)	0.167		
Size of adenomas				
Presence of adenomas (6–9 mm)	1.00(0.60–1.66)	0.995		
Characteristics of SSLs				
Number of SSLs	0.68(0.28–1.68)	0.403		
Location of SSLs				
Presence of proximal SSLs	1.49(0.47–4.77)	0.497		
Presence of distal SSLs	0.28(0.04–2.00)	0.203		
Size of SSLs				
Presence of SSLs (6–9 mm)	1.71(0.53–5.45)	0.368		

ADR Adenoma detection rate, SSL Sessile serrated lesion

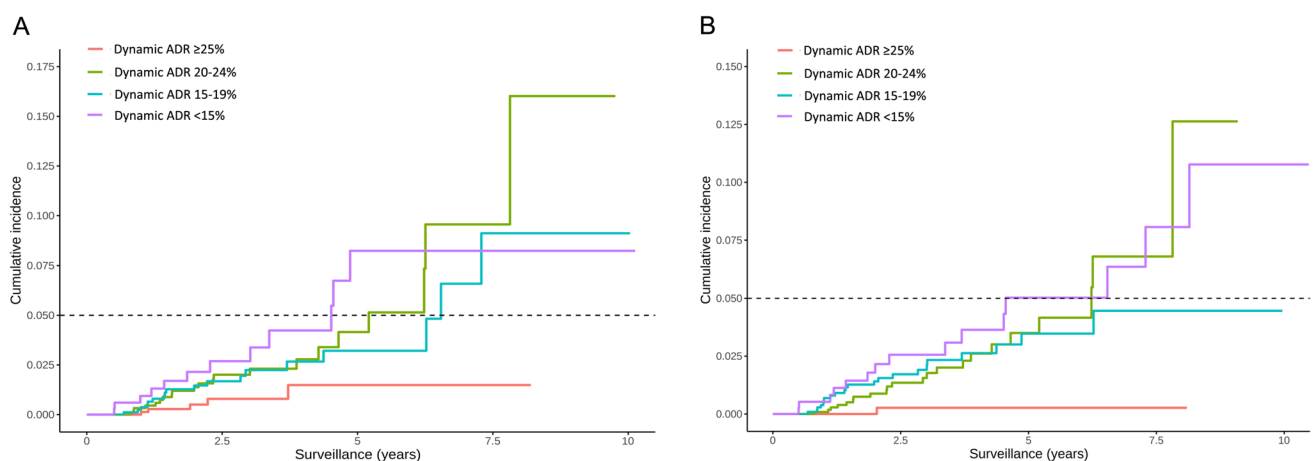
**Fig. 2** Cumulative incidence of metachronous ACRN in individuals who had removal of low-risk findings in first-time screening colonoscopy. **A** Cumulative incidence of metachronous ACRN stratified by age at baseline colonoscopy. **B** Cumulative incidence of metachro-

nous ACRN stratified by endoscopist dynamic ADR. Black dashed line, 5% threshold. ACRN, advanced colorectal neoplasia; ADR, adenoma detection rate

Table 3 Sensitivity analysis of cox-regression model for metachronous advanced neoplasia in individuals without adenomas/SSLs resection during follow-up

	Univariate		Multivariate	
	HR (95% CI)	<i>p</i> value	HR (95% CI)	<i>p</i> value
Age				
< 50 years	Reference		Reference	
50–59 years	10.5(1.40–78.8)	0.022	10.7(1.43–80.0)	0.021
60–69 years	15.2(2.06–112)	0.008	15.54(2.1–115)	0.007
≥ 70 years	23.2(3.01–178)	0.003	24.3(3.16–187)	0.002
Male gender	1.12(0.66–1.92)	0.665		
Dynamic ADR				
≥ 0.25	Reference		Reference	
0.20–0.24	3.19(1.20–8.46)	0.020	3.24(1.22–8.60)	0.018
0.15–0.19	2.67(0.99–7.21)	0.053	2.84(1.05–7.68)	0.040
< 0.15	4.07(1.42–11.7)	0.009	4.37(1.53–12.5)	0.006
Characteristics of adenomas				
Number of adenomas	1.37(0.82–2.27)	0.226		
Location of adenomas				
Presence of proximal adenomas	1.30(0.76–2.20)	0.337		
Presence of distal adenomas	0.81(0.48–1.38)	0.438		
Size of adenomas				
Presence of adenomas (6–9 mm)	1.07(0.63–1.82)	0.799		
Characteristics of SSLs				
Number of SSLs	0.74(0.30–1.81)	0.512		
Location of SSLs				
Presence of proximal SSLs	1.67(0.52–5.35)	0.386		
Presence of distal SSLs	0.30(0.04–2.19)	0.237		
Size of SSLs				
Presence of SSLs (6–9 mm)	1.88(0.59–6.04)	0.286		

ADR Adenoma detection rate, SSL Sessile serrated lesion

**Fig. 3** Sensitivity analysis of cumulative incidence of metachronous ACRN in individuals who had removal of low-risk findings in first-time screening colonoscopy. **A** Cumulative incidence of metachronous ACRN stratified by endoscopist dynamic ADR in subsets of individuals who did not have low-risk adenoma/SSLs removed during

follow-up. **B** Cumulative incidence of metachronous ACRN stratified by endoscopist dynamic ADR when the dynamic ADR was calculated from previous 200 colonoscopies. Black dashed line, 5% threshold. ACRN, advanced colorectal neoplasia; ADR, adenoma detection rate

Table 4 Sensitivity analysis of cox-regression model for metachronous advanced neoplasia, using dynamic ADR calculated from the previous 200 colonoscopies

	Univariate		Multivariate	
	HR (95% CI)	<i>p</i> value	HR (95% CI)	<i>p</i> value
Age				
< 50 years	Reference		Reference	
50–59 years	12.5(1.68–92.8)	0.014	12.4(1.67–92.2)	0.014
60–69 years	14.4(1.95–107)	0.009	14.7(1.99–109)	0.008
≥ 70 years	26.5(3.48–202)	0.002	26.8(3.52–204)	0.002
Male gender	1.01(0.60–1.69)	0.972		
Dynamic ADR				
≥ 0.25	Reference		Reference	
0.20–0.24	11.6(1.57–86.4)	0.016	11.4(1.53–84.5)	0.017
0.15–0.19	11.4(1.53–84.3)	0.018	11.5(1.54–85.3)	0.017
< 0.15	16.4(2.15–125)	0.007	17.0(2.23–130)	0.006
Characteristics of adenomas				
Number of adenomas	1.11(0.68–1.81)	0.664		
Location of adenomas				
Presence of proximal adenomas	1.26(0.76–2.11)	0.368		
Presence of distal adenomas	0.75(0.45–1.25)	0.262		
Size of adenomas				
Presence of adenomas (6–9 mm)	1.08(0.65–1.79)	0.777		
Characteristics of SSLs				
Number of SSLs	0.85(0.38–1.89)	0.688		
Location of SSLs				
Presence of proximal SSLs	1.59(0.50–5.06)	0.437		
Presence of distal SSLs	0.58(0.14–2.37)	0.445		
Size of SSLs				
Presence of SSLs (6–9 mm)	2.30(0.83–6.36)	0.108		

ADR Adenoma detection rate, SSL Sessile serrated lesion

the number of low-risk adenomas and SSLs. In addition to the bowel preparation and complete examination, the ADR was also an important indicator for the quality of colonoscopy. Previous studies have shown that the endoscopists' ADR was inversely associated with the risk of metachronous ACRN after negative colonoscopy and polypectomy [14]. A prior study using dynamic ADR, an dynamically calculated indicator reflecting the short-term ADR before the examination, found that it was a predictor for post-screening CRC after negative colonoscopy and polypectomy [12]. In this study, we used dynamic ADR in a general patient population as an endoscopist-level factor and investigated its relationship with metachronous ACRN in individuals who had low-risk findings removed in baseline colonoscopy. It was found that the individuals whose baseline colonoscopy was performed by an endoscopist with a dynamic ADR < 25% exhibited a significantly higher risk of metachronous ACRN compared with those with a dynamic ADR ≥ 25%. Further analysis showed that the cumulative incidence of metachronous ACRN reached the 5% threshold at about 5 years in the dynamic ADR < 15% group and at about 7 years in dynamic ADR 15–24% group. These results suggest that a 5-year and

a 7-year follow-up interval are optimal surveillance strategies for individuals whose baseline colonoscopy was performed by an inadequate endoscopist (dynamic ADR < 15%) and by an adequate endoscopist with a moderate dynamic ADR (15–24%), respectively. Meanwhile, the cumulative incidence of metachronous ACRN remained at a low level in the highest (≥ 25%) dynamic ADR group, which indicates that a 10-year follow-up interval is recommended for individuals whose baseline colonoscopy was performed by an endoscopist with dynamic ADR ≥ 25%.

Patient age at baseline colonoscopy has also been identified as a risk factor for metachronous ACRN. A previous study demonstrated that patients aged ≥ 50 had a higher 5-year risk of metachronous ACRN (5.9%) than patients aged 30 to 39 (2.8%) and patients aged 40 to 49 (3.3%) after the removal of low-risk adenomas [15]. However, other studies demonstrated that the incidence of metachronous ACRN did not differ significantly between young and older individuals with low-risk findings [16, 17]. In our study, a 11.3-, 15.4-, and 28.5-fold increased risk for metachronous ACRN was found in individuals aged 50–59, 60–69, and ≥ 70, respectively, compared with

individuals aged ≤ 50 . Further analysis showed that the cumulative incidence of metachronous ACRN reached the 5% threshold at about 5 years in individuals aged ≥ 70 , and at about 7 years in individuals aged 50–69, which suggests that a 5-year and a 7-year follow-up interval are suitable for individuals aged ≥ 70 and aged 50–69, respectively. A very low risk of metachronous ACRN was observed in individuals aged < 50 , which indicates that a 10-year follow-up interval is recommended for these patients.

Other clinical characteristics and endoscopic findings, including the distribution and maximum size of lesions, were also considered as potential predictors for metachronous ACRN. Some previous studies have found that the incidence of metachronous ACRN was associated with the male gender [18–20], as well as with the maximum size and anatomic distribution of lesions detected in baseline colonoscopy [21–25]. However, there were few studies focusing on the risk of metachronous ACRN in individuals with diminutive or small low-risk findings, or in those with low-risk findings detected in either the proximal or distal colon. In this study, we investigated the relationship of these potential predictors in individuals who had low-risk findings in baseline colonoscopy with metachronous ACRN. However, none of these factors were significantly associated with the risk of metachronous ACRN, which indicates that these factors are insufficient to influence the surveillance interval recommendations.

There were several limitations in our retrospective study. First, our analyses were based on the basic information of patients and endoscopic findings, which did not account for other clinical characteristics, such as BMI, smoking, and alcohol intake. Second, the median duration of follow-up in our study was short (2.34 years). However, this was partly due to the tendency of patients in our region to undergo surveillance colonoscopy early in order to detect precancerous lesions in advance, which might result in earlier endpoint and render our results more reliable.

Conclusion

In conclusion, our study showed that endoscopists' dynamic ADR and patient age at baseline colonoscopy were risk factors for metachronous ACRN in individuals who had removal of low-risk findings in first-time screening colonoscopy. A 5-year and a 7-year follow-up interval are optimal surveillance strategies for Individuals whose baseline colonoscopy was performed by an inadequate endoscopist (dynamic ADR $< 15\%$) and by an endoscopist with moderate dynamic ADR (15–24%), respectively, which were shorter than that recommended for individuals whose baseline colonoscopy was performed by an endoscopist with a dynamic ADR $\geq 25\%$ (a 10-year follow-up interval). These

findings underscore the need to emphasize the important role of endoscopist ADR, particularly short-term dynamic ADR, in determining the risk of metachronous ACRN in individuals with low-risk findings in first-time screening colonoscopy.

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Author contributions Danian Ji and Shuchang Xu designed and directed the research. Zhiyu Dong conducted a majority of the experiments and wrote the manuscript. Ouyang Li, Yanglei Li, Zili Xiao, and Feng Li planned the experiments and provided technical assistance. All authors contributed to the article and approved the submitted version.

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Data availability All data included in this study are available upon request by contact with the corresponding author.

Declarations

Disclosures Zhiyu Dong, Ouyang Li, Yanglei Li, Zili Xiao, Feng Li, Shuchang Xu, and Danian Ji declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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