ORIGINAL ARTICLE: Clinical Endoscopy

Segmental metachronous adenoma rate as a metric for monitoring incomplete resection in a colonoscopy screening program



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Background and Aims: Polypectomy technique has been shown to vary among colonoscopists, and interval colorectal cancer may result from incomplete resection of an adenoma. Methods to monitor polypectomy quality and the size of polyps resected to monitor have not been well defined. The aim of this study was to compare the rate of metachronous adenoma attributable to incomplete resection in polyps 6 to 9 mm versus polyps 10 to 20 mm.

Methods: The segmental metachronous adenoma rate attributable to incomplete resection (SMAR-IR) was calculated by subtracting the rate of metachronous neoplasia (MN) in segments without adenoma from segments with adenoma. The primary outcome of the study was the SMAR-IR in polyps 6 to 9 mm and 10 to 20 mm found on index colonoscopy.

Results: Of 337 patients included in the analysis, 146 patients had a tubular adenoma (TA) 10 to 20 mm in size and 191 patients a TA 6 to 9 mm in size as the most advanced lesion. For cases in which an index 10- to 20-mm TA was resected, the SMAR in segments with adenoma was 21.0% and in segments without adenoma 9.6%, so the SMAR-IR was 11.4% (95% confidence interval, 4.5-18.3). For cases in which an index 6- to 9-mm TA was resected, the SMAR in segments with adenoma was 22.0% and in segments without adenoma 8.8%, so the SMAR-IR was 13.2% (95% confidence interval, 7.2-19.4). Among 6 colonoscopists, the SMAR-IR ranged between 7.0% and 15.5% for polyps 6 to 20 mm.

Conclusions: MN rates in segments with a TA 10-20 mm and a TA 6-9 mm are higher than the MN rates in segments without index neoplasia. Incomplete resection of neoplasia appears to be a significant risk factor for MN in 6- to 9-mm lesions as well as larger ones. (Gastrointest Endosc 2021;94:347-54.)

Interval colorectal cancer (ICRC) is defined as CRC diagnosed after a screening or surveillance examination in which no cancer is detected and before the next recommended examination. ^{1,2} Incomplete resection of colonic polyps may play a significant role in ICRC development,

with 10% to 30% of ICRC potentially attributable to incomplete resection of polyps during a prior colonoscopy.³ An increased occurrence of ICRC from the same segment in which a polyp underwent prior endoscopic resection has been reported.⁴⁻⁶

Abbreviations: CRC, colorectal cancer; ICRC, interval colorectal cancer; MN, metacbronous neoplasia; SMAR, segmental metacbronous adenoma rate; SMAR-IR, segmental metacbronous adenoma rate attributable to incomplete resection; TA, tubular adenoma.

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Studies that use marginal biopsy samples at the polypectomy site have shown that residual neoplasia occurs in up to 23% of polypectomy snare resections among some colonoscopists.^{7,8} The clinical significance of how frequently residual neoplasia postpolypectomy suboptimal technique ultimately leads to metachronous neoplasia (MN) and contributes to ICRC risk is not well defined. Missed lesions during the index colonoscopy and de novo neoplasia with rapid development of lesions are additional etiologies of MN that might occur at the location of a prior resection.⁵ Recently, Adler et al⁹ described a method to indirectly measure MN risk from incomplete resection specifically using the absolute difference between the risk of MN from colonic segments with neoplastic polyps and the risk from segments without neoplastic polyps. Adler et al's study provides a potential method to critically assess the quality of polypectomy in a colonoscopy cohort but was limited to patients with polyps 10 to 20 mm in size and did not account for polyp removal method or variations between colonoscopists. It remains unclear which lesions should be assessed for resection completeness and whether this should be limited to lesions ≥10 mm or should additionally monitor smaller lesions. The aim of the current study was to describe the MN attributable to incomplete resection in 6- to 9-mm lesions and 10- to 20mm lesions to define whether incomplete resection is a clinically frequent occurrence in smaller polyps, as well as larger ones, that merits monitoring.

METHODS

Study design and patients

Patients with tubular adenomas (TAs) on index colonoscopy at an academic medical center were included in the study. Pathology reports were collected by a natural language search using the term "adenoma" between January 2006 and October 2018. All pathology reports were subsequently manually reviewed to determine study inclusion. Patients with at least 1 TA between 6 and 20 mm in size identified on index colonoscopy were included.

We identified 1527 patients between January 2006 and October 2018 who underwent index colonoscopy and were found to have at least 1 TA between 6 and 20 mm. We excluded patients who had a family history of CRC before age 60 years, inflammatory bowel disease, prior CRC, colonic resection, CRC diagnosis on index colonoscopy, and lacked subsequent surveillance colonoscopy. We also excluded patients in which a TA <6 mm or >20 mm was the most advanced lesion, who had an incomplete index colonoscopy, with ≥2 polyps of the most advanced sized lesion in the same segment, and with a follow-up colonoscopy <6 months or >10 years. Follow-up colonoscopy was complete (cecal intubation and at least adequate prepration) in 98.2% of cases. Colonoscopy

was performed using 180 and 190 series colonoscopes (Olympus America Inc, Center Valley, Pa, USA).

Data collection

Endoscopy reports of patients with polyps during the study period were reviewed, and patients with at least 1 TA on index colonoscopy were identified. Patient demographics, polyp characteristics, and pathology findings were abstracted through chart review of electronic medical records. Polyp characteristics such as endoscopic size, segment location, morphology (pedunculated or nonpedunculated), removal method (snare cautery, cold snare, cold forceps, or hot forceps), resection type (en bloc or piecemeal), and the presence of advanced histologic features such as villous or high-grade dysplasia were included.

Analytic approach

Our analysis was based on the approach reported by Adler et al. We assumed that a particular segment with a completely resected adenoma had an overall risk (*R*) of metachronous adenoma equal to the sum of the metachronous adenoma risks (*R*) because of de novo adenoma formation, incomplete adenoma resection, and missed adenoma. The segmental metachronous adenoma rate (SMAR) is defined as follows:

$$R_{\text{metachronous (segment with adenoma)}} = R_{\text{(de novo)}} + R_{\text{(incomplete)}} + R_{\text{(missed)}}$$

In the segments where no adenomas were identified on index colonoscopy, the overall risk of metachronous adenoma is the sum of the risks because of de novo adenoma formation and missed adenoma, as follows:

$$R_{\text{metachronous (segment without adenoma)}} = R_{\text{(de novo)}} + R_{\text{(missed)}}$$

Based on above equations, the risk of segmental metachronous adenoma because of incomplete resection equals the risk difference between the risk in a segment with adenoma and the risk in a segment without adenoma. Therefore, the SMAR attributable to incomplete resection (SMAR-IR) is calculated as follows:

$$R_{
m (incomplete)} = R_{
m metachronous \, (segment \, with \, adenoma)}$$
 $-R_{
m metachronous \, (segment \, without \, adenoma)}$

For example, if the SMAR in a segment with an adenoma on index colonoscopy was 20% and the SMAR in a segment without adenoma on index colonoscopy was 10%, the SMAR-IR would be 10%. Therefore, higher SMAR-IR indicates more likely that the adenoma was incompletely resected.

Study outcomes

Patients were divided into 2 groups based on the findings of index colonoscopy: Group A comprised patients with at least 1 TA 10 to 20 mm in size as the most advanced lesion, whereas group B comprised patients with at least 1 TA 6 to 9 mm in maximum size as the most advanced lesion. We excluded patients who underwent follow-up

colonoscopy in <6 months or >5 years in group A and <6 months or >10 years in group B. Segments with sessile serrated adenoma/polyp were excluded from the analysis.

The primary outcome of the study was the SMAR-IR, which was calculated by subtracting the risk rate of metachronous adenoma in a segment without adenoma on index examination from the risk rate of metachronous adenoma in a segment with adenoma on index examination. We also reported the segmental metachronous advanced neoplasia rate for each group. Advanced neoplasia included adenomas with any advanced features (≥10 mm in size, villous histology, or high-grade dysplasia) and CRC. Each colonoscopy contributed 6 segments (cecum, ascending colon/hepatic flexure, transverse colon/splenic flexure, descending colon, sigmoid colon, and rectum).

Furthermore, we stratified data by the individual colonoscopist performing the index colonoscopy and reported SMAR and SMAR-IR based on follow-up colonoscopy results. To evaluate the impact of the snare resection method (snare cautery and cold snare) on the SMARs, we reported these rates separately. Each colonoscopist at our center performed over 100 colonoscopies annually, and all colonoscopists were board-certified gastroenterologists. In previous studies on the performance of our colonoscopists, the group adenoma detection rate ranged between 29.6% and 30.9% among participating colonoscopists. ^{10,11}

We included in the analysis all segments with 10- to 20-mm or 6- to 9-mm TAs as the most advanced lesion even if the segment included other smaller adenomas. In addition, we reported the SMAR and SMAR-IR for segments with 10-to 20-mm or 6- to 9-mm TAs without smaller adenomas in the same segment.

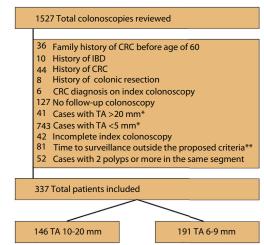
Statistical analysis

We reported continuous variables as means with standard deviation and categorical variables as frequencies and rates. We performed univariate analysis to report odds ratios (ORs) and 95% confidence intervals (CIs). SMAR-IR was reported as a rate with 95% CIs. All statistical analyses were performed using STATA/IC (version 14.2; StataCorp LLC, College Station, Tex, USA). The study was approved by the Institutional Review Board at Rush University Medical Center.

RESULTS

Patient characteristics

A total of 1527 colonoscopies were reviewed, of which 337 patients were included in the analysis: 146 patients in group A and 191 patients in group B (Fig. 1). The mean age was 60.5 years (standard deviation, 9.6), and 52.2% of patients were women. Most patients were white (56.7%), followed by African American (33.4%), and Hispanic (6.3%). The overall mean time to follow-up colonoscopy was 46.2 months (standard deviation, 2.7) (Table 1).



- *As the most advanced lesion
- ** Time to surveillance criteria was 6 months to 5 years for cases with TA 10-20 mm and 6 months an over for cases with TA 6-9 mm

Figure 1. Flow diagram of patient exclusions. *CRC*, Colorectal cancer; *IBD*, inflammatory bowel disease; *TA*, tubular adenoma.

SMAR in patients with 10- to 20-mm TA

One hundred forty-six patients contributed 157 segments with a baseline TA 10 to 20 mm, 65 segments with adenomas 1 to 9 mm, and 654 segments without adenoma on baseline colonoscopy (Table 2). The SMAR was 9.6% in segments without adenoma and 21.0% in segments with a TA 10 to 20 mm; therefore, the SMAR-IR was 11.4%. Most polyps (93.2%) were removed with snare cautery, and the SMAR-IR was 10.0% when snare cautery was used. Polyps removed with snare cautery had 2.3 times higher odds for metachronous adenoma compared with segments without adenoma (OR, 2.3; 95% CI, 1.4-3.7).

In regard to morphology, the SMAR-IR for pedunculated and nonpedunculated polyps was 11.8% and 17.0%, respectively. Nonpedunculated polyps had higher odds for metachronous adenoma than pedunculated polyps in comparison with segments without adenoma on index colonoscopy (OR, 3.4 [95% CI, 2.1-5.5] and OR, 2.6 [95% CI, 1.2-5.6], respectively). Snare cautery was used in 136 polyps (93.2%). Cold snare was used to remove 8 polyps and cold forceps in 2 polyps; therefore, the assessment for SMAR-IR was limited by small sample size in this group.

In the cohort of patients with 10- to 20-mm colonic adenomatous polyps, the segmental metachronous advanced neoplasia rate in segments without adenoma was 3.1% and in segments with adenoma was 6.4%. Therefore, the segmental metachronous advanced neoplasia rate attributable to incomplete resection was 3.3%.

SMAR in patients with 6- to 9-mm TA

One hundred ninety-one patients contributed 209 segments with TA 6 to 9 mm as the most advanced lesion, 46 segments with adenomas 1 to 5 mm, and 891 segments without adenoma on baseline colonoscopy (Table 3). Segments without adenoma on baseline colonoscopy had

TABLE 1. Characteristics of patients undergoing polypectomy of lesions 6-20 mm with recurrent surveillance colonoscopy

		<u> </u>
All patients (n = 337)	Group A (n = 146)	Group B (n = 191)
60.5 (9.6)	61.4 (10.5)	59.7 (8.8)
190 (56.7)	83 (57.2)	107 (56.3)
112 (33.4)	50 (34.5)	62 (32.6)
21 (6.3)	7 (4.8)	14 (7.4)
3 (.9)	0	3 (1.6)
9 (2.7)	5 (3.5)	4 (2.1)
176 (52.2)	71 (48.6)	90 (47.1)
161 (47.8)	75 (51.4)	101 (52.9)
29.6 (6.6)	29.1 (6.3)	29.9 (6.8)
46.2 (22.7)	33.6 (13.7)	55.9 (23.5)
	60.5 (9.6) 190 (56.7) 112 (33.4) 21 (6.3) 3 (.9) 9 (2.7) 176 (52.2) 161 (47.8) 29.6 (6.6)	60.5 (9.6) 61.4 (10.5) 190 (56.7) 83 (57.2) 112 (33.4) 50 (34.5) 21 (6.3) 7 (4.8) 3 (.9) 0 9 (2.7) 5 (3.5) 176 (52.2) 71 (48.6) 161 (47.8) 75 (51.4) 29.6 (6.6) 29.1 (6.3)

Values are n (%) unless otherwise defined. Group A, patients with a TA 10-20 mm in size as the most advanced lesion; group B, patients with a TA 6-9 mm in size as the most advanced lesion.

TABLE 2. SMARs among patients with a 10- to 20-mm TA on baseline colonoscopy (n = 146*)

	No. of segments	SMAR n (%)	Risk for any TA OR (95% CI)	SMAR-IR % (95% CI)	
Segments without neoplasia	654	63 (9.6)	1.00 (reference)	_	
Segments with a TA 10-20 mm	157	33 (21.0)	2.5 (1.6-3.9)	11.4 (4.5-18.3)	
Characteristics of TA 10-20 mm					
Nonpedunculated	113	30 (26.6)	3.4 (2.1-5.5)	17.0 (8.3-25.8)	
Pedunculated	42	9 (21.4)	2.6 (1.2-5.6)	11.8 (-1 to 24.7)	
Resection					
En bloc	154	33 (21.4)	33 (21.4) 2.6 (1.6-4.1)		
Piecemeal	3	0	_	_	
Histology					
Low-grade dysplasia	112	26 (23.2)	2.8 (1.7-4.7)	13.6 (5.3-21.9)	
Villous	34	6 (17.7)	2.0 (.8-5.0)	8.1 (-5.1 to 21.2)	
High-grade dysplasia	11	1 (9.1) .9 (.1-7.4)		5 (-17.7 to 16.7)	
Removal method					
Snare cautery	138	27 (19.6)	2.3 (1.4-3.7)	10.0 (2.8-17.0)	
Cold snare	8	2 (25.0)	3.1 (.6-15.8)	15.4 (-15.4 to 46.4)	
Cold forceps	2	1 (50.0)	9.4 (.6-151.8)	40.4 (-40.3 to 125.9)	

SMAR, Segment metachronous adenoma rate; OR, odds ratio; CI, confidence interval; TA, tubular adenoma.

a SMAR of 8.8%, whereas segments with TA 6 to 9 mm had a SMAR of 22.0%. The SMAR-IR in segments with 6- to 9-mm TAs was 13.2%. Segments with 6- to 9-mm TAs had 2.9 times higher odds for metachronous adenoma compared with segments without adenoma. Polyps that were resected en bloc had a SMAR-IR of 12.0%, and polyps resected in piecemeal had a SMAR-IR of 48.3%.

In regard to the removal method, the SMAR-IR for polyps removed with snare cautery and cold snare was 12.8% and

10.6%, respectively. The odds of metachronous adenoma in snare cautery and cold snare resections were similar (OR, 2.9 [95% CI, 1.6-5.2] and OR, 2.5 [95% CI, 1.1-5.9], respectively). On the other hand, the SMAR-IR for polyps removed with cold forceps was 16.5%, which was higher than by snare (snare cautery, 12.8%; cold snare, 10.6%). Cold forceps polypectomy of 6 to 9 mm had statistically significant higher odds for metachronous adenoma compared with segments without adenoma (OR, 3.5; 95% CI, 2.0-6.3).

^{*}Sixty-five segments with adenomas 1-9 mm are not reported in the table.

ABLE 3. SMARs among patients with a 6- to 9-mm TA on baseline colonoscopy (n $= 191*$)						
	No. of segments	Risk for any TA SMAR n (%) OR (95% CI)		SMAR-IR % (95% CI)		
Segments without neoplasia	891	78 (8.8)	1.00 (reference)	_		
Segments with a TA 6-9 mm	209	46 (22.0)	2.9 (1.9-4.4)	13.2 (7.2-19.4)		
Characteristics of TA 6-9 mm						
Resection						
En bloc	202	42 (20.8)	2.7 (1.8-4.1)	12.0 (6.1-18.1)		
Piecemeal	7	4 (57.1)	4 (57.1) 13.9 (3.1-63.2)			
Histology						
Low-grade dysplasia	196	42 (21.4)	2.8 (1.9-4.3)	12.6 (6.6-18.9)		
Villous	11	3 (27.3)	3.9 (1.1-15.1)	18.5 (-8.6 to 46.1)		
High-grade dysplasia	2	1 (50.0) 10.4 (.6-168.2)		41.2 (-40.9 to 127.6)		
Removal method						
Cold forceps	75	19 (25.3)	3.5 (2.0-6.3)	16.5 (6.4-27.1)		
Snare cautery	74	16 (21.6)	2.9 (1.6-5.2)	12.8 (3.2-22.7)		
Cold snare	36	7 (19.4)	2.5 (1.1-5.9)	10.6 (-2.5 to 23.9)		
Hot forceps	6	1 (16.7)	2.1 (.2-18.0)	7.9 (-22.2 to 38.1)		

SMAR, Segment metachronous adenoma rate; OR, odds ratio; CI, confidence interval; TA, tubular adenoma

In the cohort of patients with a maximum size polyp of 6 to 9 mm, the segmental metachronous advanced neoplasia rate in segments without adenoma was 2.1% and in segments with adenoma was 4.3%. Therefore, the segmental metachronous advanced neoplasia rate attributable to incomplete resection was 2.2%.

SMAR by colonoscopist

We identified 17 individual colonoscopists who performed index colonoscopies. We reported the SMAR and SMAR-IR for colonoscopists who performed 25 colonoscopies or more with resections of 6- to 20-mm lesions. The SMAR among colonoscopists was reported for all 6to 20-mm included resected lesions (Table 4). We also evaluated the SMAR for polyps only removed by snare polypectomy, excluding forceps removal (Table 4). Among 6 included colonoscopists there were 289 segments with 6- to 20-mm TA, and the SMAR was 21.1%. The range of SMAR was between 16.7% (colonoscopist D) and 24.3% (colonoscopist B). The overall SMAR-IR was 11.9% and ranged between 7.0% and 15.5%. When limiting analysis to only those removed by snare, the aggregate SMAR was 20.6% with a range of 15.5% (colonoscopist D) and 26.7% (colonoscopist F). The average SMAR-IR in this subgroup was 11.4%, ranging between 5.8% and 17.9%.

SMAR calculation in patients with 6- to 20-mm TA with and without inclusion of smaller adenomas in the same segment

Segments with a TA 10 to 20 mm only without other smaller adenomas had a SMAR-IR of 11.1%. In comparison

with the SMAR-IR of the segments with 10- to 20-mm TA including smaller adenomas in the same segment (11.4%), the difference between these rates was negligible at .3%. Similarly, segments with a TA 6 to 9 mm only without smaller adenomas had a SMAR-IR of 10.5%, whereas the SMAR-IR inclusive of smaller adenomas was 13.2%, or 2.7% higher (Table 5).

SMAR by proximal versus distal location

Among patients with a 10- to 20-mm TA in the proximal colon, the SMAR in segments without adenoma on baseline colonoscopy was 15.2% and in segments with a TA 10 to 20 mm was 32.6% (Fig. 2). Therefore, the SMAR-IR of segments with a 10- to 20-mm TA in the proximal colon was 17.4%. In the distal colon, the SMAR in segments without adenoma on baseline colonoscopy was 4.8% and in segments with a 10- to 20-mm TA was 5.9%, so the SMAR-IR was 1.1%.

Among patients with a 6- to 9-mm TA the proximal colon, the SMAR in segments without adenoma was 12.6% and in segments with a 6- to 9-mm TA was 31.0%; therefore, the SMAR-IR was 18.4% (Fig. 2). In the distal colon, the SMAR in segments without adenoma was 5.3% and in segments with a 6- to 9-mm TA was 8.4%, so the SMAR-IR was 3.1%.

DISCUSSION

We evaluated the risk of MN because of incomplete resection among patients with a TA 6 to 20 mm. The SMAR-IR was 11.4% in patients with a 10- to 20-mm TA

^{*}Forty-six segments with adenomas 1-5 mm are not shown in the table.

TABLE 4. SMARs based on follow-up colonoscopy results by colonoscopist and removal method

		Forceps and	snare polypect	omy	Snare		
Colonoscopist	Total no. of patients	No. of segments with TA 6-20 mm	SMAR n (%)	SMAR-IR (%)	No. of segments with TA 6-20 mm	SMAR n (%)	SMAR-IR (%)
Α	34	38	8 (21.1)	14.0	28	7 (25.0)	17.9
В	66	70	17 (24.3)	15.5	59	13 (22.0)	13.2
С	30	35	8 (22.8)	13.2	28	6 (21.4)	11.8
D	73	78	13 (16.7)	7.0	58	9 (15.5)	5.8
E	29	32	7 (21.9)	14.4	21	4 (19.0)	11.6
F	33	36	8 (22.2)	9.8	15	4 (26.7)	14.3
Total	265	289	61 (21.1)	11.9	209	43 (20.6)	11.4

SMAR, Segment metachronous adenoma rate; SMAR-IR, segmental metachronous adenoma rate attributable to incomplete resection; TA, tubular adenoma.

TABLE 5. SMARs among patients with a 10- to 20-mm TA and a 6- to 9-mm TA only without smaller adenomas in the same segment on baseline colonoscopy

No. of patients with a TA 10-20 mm = 120	No. of segments	SMAR n (%)	SMAR-IR % (95% CI)
Segments without neoplasia	542	47 (8.7)	_
Segments with a TA 10-20 mm only (no other adenoma <10 mm in the same segment)	126	25 (19.8)	11.1 (3.7-18.7)
Segments with a TA 10-20 mm including smaller adenomas in the same segment	157	33 (21.0)	11.4 (4.5-18.3)
No. of patients with a TA 6-9 mm = 160			
Segments without neoplasia	748	64 (8.6)	_
Segments with a TA 6-9 mm only (no other adenoma <6 mm in the same segment)	173	33 (19.1)	10.5 (4.3-16.8)
Segments with a TA 6-9 mm including smaller adenomas in the same segment	209	46 (22.0)	13.2 (7.2-19.4)

SMAR, Segment metachronous adenoma rate; SMAR-IR, segmental metachronous adenoma rate attributable to incomplete resection; TA, tubular adenoma; CI, confidence interval.

(group A) and 13.2% in patients with a 6- to 9-mm TA (group B). Segments without neoplasia in groups A and B had similar SMARs of 9.6% and 8.8%, respectively. The similar SMAR-IR-derived calculated findings in TAs 10 to 20 mm was similar to the rate in TAs 6 to 9 mm. Thus, a major finding of this study is that the contribution of MN as described by the SMAR-IR appears to be significant in not only lesions \geq 10 mm but also in those of 6 to 9 mm in size in our cohort. The reported SMAR-IR in group A of 11.4% was similar to the reported rate by Adler et al (10.3%) for 10- to 20-mm polyps, showing that this is a relatively reproducible rate between the cohorts.

Of the adenomas on follow-up colonoscopy, 54% of all adenomas could potentially be attributed to incomplete resection in TAs 10 to 20 mm and 60% of all adenomas could potentially be attributed to incomplete resection in TAs 6 to 9 mm. Thus, and surprisingly, more than half of the metachronous adenomas might potentially occur because of incomplete resection in both groups. This suggests that the predisposition of MN attributed to prior adenoma that drives our surveillance recommendations may to a greater extent than previously appreciated be driven by incomplete resection. These results emphasize the

importance of completeness in resection for adenomas in the 6- to 20-mm range.

We showed that the resection of adenoma correlated with a future modest increase in metachronous advanced neoplasia at that segment. The segmental metachronous advanced neoplasia rate attributable to incomplete resection was 2.2% in the 6- to 9-mm group and 3.3% in the 10- to 20-mm group. The clinical significance of this modest metachronous advanced neoplasia increase and its actual impact on ICRCs is unclear and deserves further evaluation in larger adequately powered studies.

In 2 randomized clinical trials for small and diminutive adenomas, cold snare polypectomy achieved higher complete resection rates compared with cold forceps polypectomy, and it was an independent factor for complete resection. ^{12,13} In a recent systematic review and metanalysis study of polyps 1 to 20 mm in size that were removed by snare, the incomplete resection rate was 13.8%. ¹⁴ In polyps 1 to 5 mm in size, the forceps incomplete resection rate was higher than the snare rate (9.9% vs 4.4%). In our study, the SMAR-IR for 6- to 9-mm TAs that were removed with cold forceps was higher than those removed by snare cautery or cold snare

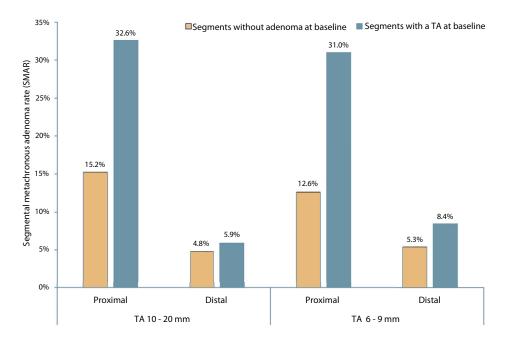


Figure 2. Segmental metachronous adenoma rates by location. TA, Tubular adenoma.

(16.5% vs 12.8% vs 10.6%, respectively). Thus, our study shows that the method of removal of small polyps, which predisposes to incomplete resection, actually has long-term negative consequences in terms of MN. These findings are in line with the recommendations of the European Society of Gastrointestinal Endoscopy and the U.S. Multi-Society Task Force on Colorectal Cancer for using cold snare to remove small polyps (<10 mm) rather than using forceps in these lesions. ^{15,16} The methodology of SMAR-IR calculation as described here shows how the method of polyp removal can be evaluated for comparative efficacy over time by measuring metachronous adenoma burden.

The variation among colonoscopists when applying SMAR-IR as a quality metric for monitoring polypectomy completeness on the specific colonoscopist level is not defined. In our cohort comparing 6 colonoscopists, the SMAR-IR ranged between 7.0% and 15.5% for polyps 6 to 20 mm. Thus, rates that exceed that range in our monitoring could be considered to merit further investigation of polypectomy technical performance or technique decision-making.

In terms of methodology of SMAR-IR calculation, we considered 2 different approaches, 1 in which smaller adenomas at the same segment would be included versus excluded because they may also be a potential source of recurrence. By excluding smaller adenomas at the concomitant segment, the difference in the SMAR-IR in segments with a 10- to 20-mm TA was only .3%, whereas the difference was 2.7% in segments with a 6- to 9-mm TA. In this cohort the SMAR-IR was minimally impacted by the presence of smaller concomitant adenomas. This makes the

calculation easier to implement in practice because any case with a polyp of 6 to 20 mm can essentially be included without adjustment for presence of concomitant smaller adenomas. In regard to the location of polyps in the colon, incomplete resection rates were higher in the proximal colon compared with the distal colon. Thus, further studies might consider a more targeted assessment of right-sided SMAR-IR.

The study has several limitations. First, the methodology of calculating SMAR-IR does not account for a field defect predisposing to recurrent neoplasia preferentially in the segment of prior resection. However, the difference in SMAR-IR based on resection technique as shown here makes it unlikely to make field defect a large contributor to the effect. Second, the SMAR-IR relies on the accurate endoscopic identification of polyp segment location, and therefore our rates of SMAR-IR may be affected by identifying the segment and may be underestimated. Third, the clinical significance of potential residual neoplasia recurrence attributable to incomplete resection is unclear, and the extent to which this is truly a precursor to ICRC deserves further study. However, we did show a modest increase in metachronous advanced neoplasia at the segment of prior resection of lesions 6 to 20 mm in size. Fourth, the morphology of polyps 6 to 9 mm in size found on index colonoscopy was not reported in all cases, and therefore we did not include these data in the analysis. An alternative future monitoring methodology approach that could potentially be simpler to implement at the level of the colonoscopist would track total metachronous adenoma burden changes over time irrespective of segment location, although this would still be based on the assumption that an adenoma detection rate stayed similar over time.

There are several strengths of the study. First, we used an assessment that considered the presence of smaller adenomas in the calculation for SMAR-IR, showing that they did not significantly impact the SMAR-IR. Second, we showed in a real-life situation how the technical method of polypectomy selection can be compared using recurrent adenoma data rates as shown in forceps versus snare removal in 6- to 9-mm TAs. Third, we showed rates of SMAR-IR variation among colonoscopists for which future studies can contrast in further developing metrics for polyp resection efficacy. Finally, we showed that SMAR-IR appears to occur in lesions 6 to 9 mm in size at a significant rate, and monitoring of lesions of this size should be considered.

In summary, we showed that SMAR-IR is a promising metric in monitoring retrospectively polypectomy quality. The main finding of this study was that the recurrence from incomplete resection appears to occur in 6- to 9-mm lesions at a rate similar to larger lesions among our cohort. The extent to which this can be reduced by resection technique education and monitoring deserves further study. The methodology as described here can be used to contrast resection techniques for completeness of resection and can offer guidance on the efficacy of specific polypectomy technique approaches. Further studies in prospective cohorts could consider defining the cutoff of SMAR-IR as a quality target in those performing high-quality polypectomy.

REFERENCES

- Sanduleanu S, le Clercq CM, Dekker E, et al. Definition and taxonomy of interval colorectal cancers: a proposal for standardising nomenclature. Gut 2015;64:1257-67.
- Rutter MD, Beintaris I, Valori R, et al. World Endoscopy Organization consensus statements on post-colonoscopy and post-imaging colorectal cancer. Gastroenterology 2018;155:909-25.

- Adler J, Robertson DJ. Interval colorectal cancer after colonoscopy: exploring explanations and solutions. Am J Gastroenterol 2015;110: 1657-64.
- Samadder NJ, Curtin K, Tuohy TM, et al. Characteristics of missed or interval colorectal cancer and patient survival: a population-based study. Gastroenterology 2014;146:950-60.
- Robertson DJ, Lieberman DA, Winawer SJ, et al. Colorectal cancers soon after colonoscopy: a pooled multicohort analysis. Gut 2014;63: 949-56.
- Brenner H, Chang-Claude J, Jansen L, et al. Role of colonoscopy and polyp characteristics in colorectal cancer after colonoscopic polyp detection: a population-based case-control study. Ann Intern Med 2012;157:225-32.
- Pohl H, Srivastava A, Bensen SP, et al. Incomplete polyp resection during colonoscopy—results of the Complete Adenoma Resection (CARE) study. Gastroenterology 2013;144:74-80.
- Kawamura T, Takeuchi Y, Asai S, et al. A comparison of the resection rate for cold and hot snare polypectomy for 4-9 mm colorectal polyps: a multicentre randomised controlled trial (CRESCENT study). Gut 2018;67:1950-7.
- Adler J, Toy D, Anderson JC, et al. Metachronous neoplasias arise in a higher proportion of colon segments from which large polyps were previously removed, and can be used to estimate incomplete resection of 10-20 mm colorectal polyps. Clin Gastroenterol Hepatol 2019;17: 2277-84.
- Greenspan M, Rajan KB, Baig A, et al. Advanced adenoma detection rate is independent of nonadvanced adenoma detection rate. Am J Gastroenterol 2013;108:1286-92.
- Melson J, Berger D, Greenspan M, et al. Maintaining low nonneoplastic polypectomy rates in high-quality screening colonoscopy. Gastrointest Endosc 2017;85:581-7.
- Lee CK, Shim JJ, Jang JY. Cold snare polypectomy vs. cold forceps polypectomy using double-biopsy technique for removal of diminutive colorectal polyps: a prospective randomized study. Am J Gastroenterol 2013;108:1593-600.
- Kim JS, Lee BI, Choi H, et al. Cold snare polypectomy versus cold forceps polypectomy for diminutive and small colorectal polyps: a randomized controlled trial. Gastrointest Endosc 2015;81:741-7.
- 14. Djinbachian R, Iratni R, Durand M, et al. Rates of incomplete resection of 1- to 20-mm colorectal polyps: a systematic review and meta-analysis. Gastroenterology 2020;159:904-14.
- Ferlitsch M, Moss A, Hassan C, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. Endoscopy 2017;49:270-97.
- Kaltenbach T, Anderson JC, Burke CA, et al. Endoscopic removal of colorectal lesions-recommendations by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2020;158:1095-129.