

# Evaluating outcomes of alternative pathologic terminology in high-grade dysplastic colorectal lesions

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## Abstract

**Background** Pathologists occasionally classify colorectal adenomas with dysplastic mucosal invasion as intramucosal carcinoma (IMC), or carcinoma *in situ* (CIS), instead of high-grade dysplasia (HGD), potentially leading to earlier surveillance colonoscopies and inappropriate surgical referrals. We aimed to analyze differences in the management of patients with these diagnoses, and examined the factors that may lead to inappropriate early interval (IEI) follow-up recommendations for surveillance.

**Methods** We reviewed 870 colonoscopy and pathology reports from 2015-2022, excluding cases of colorectal cancer, inflammatory bowel disease, and lesions not amenable to endoscopic resection. Surveillance appropriateness was defined in accordance with the 2020 US Multi Society Task Force (USMSTF) guidelines. ANOVA and Fisher's exact tests were used to compare patient groups, while binary logistic regression identified predictors of IEI.

**Results** Among 233 patients analyzed, 86% had HGD, 12% IMC and 2% CIS. IMC (odds ratio [OR] 4.09, 95% confidence interval [CI] 1.52-11.5; P=0.01) and CIS (OR 3.70, 95%CI 0.57-29.7; P=0.17) had significantly higher IEI rates relative to HGD. Predictors of IEI included Black race (OR 2.39, 95%CI 1.17 - 5.03; P=0.02), *en bloc* resection (OR 10.9, 95%CI 3.53-49.0; P<0.001), and IMC (OR 4.09, 95%CI 1.52-11.50; P=0.01). No differences in surveillance outcomes were observed.

**Conclusions** Endoscopic resection is curative for dysplasia confined to the mucosa in completely resected colonic adenomas. Labeling these lesions as "carcinoma" increases IEI recommendations without improving outcomes. Our findings support the 2020 USMSTF guidelines to standardize all dysplastic colorectal lesion terminology as HGD to ensure appropriate follow-up intervals.

**Keywords** High-grade dysplasia, intramucosal carcinoma, carcinoma *in situ*, surveillance colonoscopy, colorectal cancer

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## Introduction

Colorectal cancer (CRC) is the third most diagnosed cancer in the United States (US), and the second leading

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cause of combined cancer-related deaths in men and women; it was predicted to cause approximately 52,900 deaths during 2025 [1]. It has been well established that normal screening colonoscopy in patients with average risk is associated with sustained risk reduction for both incident and fatal CRC [2,3]. However, the risk of incident and fatal CRC after adenoma removal remains uncertain [4-8].

High-grade dysplasia (HGD) in colorectal adenomas is a histologic diagnosis characterized by marked architectural and cytologic atypia limited to the epithelium, including crowded and complex glandular architecture, cribriform patterns, loss of cellular polarity, irregular hyperchromatic nuclei, and atypical mitotic figures [9]. Although HGD in colonic adenoma is a relatively rare finding, some studies suggest that it is a risk factor for interval CRC [10,11]. Instead of HGD, pathologists often use the term "carcinoma *in situ*" (CIS) to describe dysplasia that is still within the epithelium and "intramucosal carcinoma" (IMC) to describe dysplasia that invades the *lamina propria* or the *muscularis mucosa*, but does

not cross into the submucosa (i.e., remains within the mucosa). This terminology is based on the revised Vienna classification, an older nomenclature system developed in 2002 to classify all types of gastrointestinal intramucosal neoplasia [12,13].

CIS or IMC in the colorectum are generally agreed to be synonymous with HGD, as they are thought to not have any metastatic potential [9,14-16]. This differs from the definition of invasive carcinoma in other parts of the gastrointestinal tract (esophagus, stomach and small intestine), where the presence of mucosal invasion is sufficient for the diagnosis of invasive cancer (pT1) [17,18]. The National Comprehensive Cancer Network (NCCN) classifies all dysplastic colorectal adenomas limited to the mucosa as “Tis” (*in situ*) [18]. Endoscopic resection is curative for all Tis adenomas of the colon, and a surveillance strategy of 3 years should suffice if these are resected *en bloc* with clear margins [19,20]. Accordingly, T staging or Tis is rarely used for adenomas in clinical practice. It is recommended by the US Multi-Society Task Force (USMSTF) on CRC that all dysplastic adenomas confined to the mucosa should be described as HGD, and that CIS or IMC should not be used to describe these precancerous lesions, to avoid unnecessary confusion and anxiety [17]. IMC and CIS are rare diagnoses in relation to colorectal adenomas, and to the best of our knowledge no studies have evaluated the impact of follow-up recommendations after these diagnoses when compared to HGD.

The primary aim of our study was to analyze differences in the management of patients at our institution who were reported to have colonic adenomas with IMC or CIS, vs. those with HGD. The secondary aim was to analyze the difference in outcomes for those who were recommended surveillance at appropriate vs. inappropriate intervals after resection of a Tis colorectal adenoma at their next surveillance colonoscopy. The tertiary aim was to analyze any differences in patient and endoscopic characteristics, and to identify predictors for IEI.

## Patients and methods

This was a single-center retrospective analysis conducted at the MetroHealth Medical Center (MHMC) in Cleveland, Ohio, US. MHMC is a tertiary care academic medical center and serves as a safety-net institution for approximately 300,000 people in northeastern Ohio. MHMC serves a large and diverse population, including a significant proportion of underinsured patients. We

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performed a retrospective chart review of colonoscopies and pathology reports from January 2015 to December 2022. The colonoscopies were performed at MHMC and 2 of its satellite community hospitals by board-certified gastroenterologists. This study was approved by the MHMC institutional review board.

We reviewed 870 colonoscopy and pathology reports of patients with a diagnosis of either HGD, IMC or CIS, excluding cases of low-grade dysplasia. All pathology reporting was carried out by board-certified pathologists at a central location. Internal review was performed by a second board-certified pathologist specializing in gastrointestinal pathology for confirmation of IMC and CIS. HGD cases did not undergo an internal review process unless there was concern about deeper invasion. After excluding patients with a personal or family history of CRC, CRC syndromes, inflammatory bowel disease (IBD) and lesions not amenable to endoscopic resection (large masses >60 mm, features of invasive cancer such as depression or non-lifting sign), we included 233 patients in our analysis. None of the patients we included had multiple (>1) lesions. Appropriate surveillance intervals were determined, based on the 2020 USMSTF recommendations. For lesions with *en bloc* resection and clear margins on pathology, the appropriate surveillance interval (ASI) was defined as 3 years. For lesions >20 mm that were removed via piecemeal resection, the ASI was defined as 6 months. Recommendations for surveillance earlier than these intervals were defined as inappropriate early intervals (IEI). Surveillance recommendations were retrieved from the electronic medical records of the included patients, based on the endoscopist's documented plan following pathology review. Patients who were recommended a colonoscopy at an earlier interval for other valid reasons such as >10 polyps/adenomas, concern about residual polyp, piecemeal resection of another polyp in the same examination, and inadequate or poor bowel prep were not included in the IEI group.

## Statistical analysis

Data were collected in MS Excel by selecting from a standardized drop-down with discrete, pre-defined entities for each variable to limit observer bias. We compared demographics, endoscopic characteristics and differences in follow up amongst patients with HGD, IMC and CIS, using analysis of variance (ANOVA) and Fisher's exact omnibus tests, as well as Agresti standardized residuals *post hoc* tests. Outcomes at the next surveillance colonoscopy in both ASI and IEI groups were defined as interval polyp(s) or CRC. A univariate analysis of differences in demographics, endoscopic characteristics, pathology and outcome between the 2 groups was performed using ANOVA and Fisher's exact tests for continuous and categorical variables, respectively. Binary logistic regression was performed on the strongest and most clinically plausible univariate predictors to avoid overfitting, given the limited number of IEI events.

## Results

### Baseline characteristics of study population

A total of 233 patients were included in our study, of whom 200 (86%), 28 (12%) and 5 (2%) had HGD, IMC and CIS, respectively. No statistically significant differences were observed in demographics or endoscopic characteristics among the HGD, IMC, and CIS groups (Table 1). The mean age at diagnosis was 64.6±9.98 years for HGD, 61.4±10 years for IMC and 65.2±9.34 years for CIS. Males comprised 60% of the HGD and CIS groups, and 50% of the IMC group. HGD was slightly more prevalent among White patients (49%), whereas IMC was more common in Black patients (46%). Most lesions were found in the rectosigmoid colon, accounting for 57.5% of HGD, 82% of IMC and 80% of CIS cases. Polyp morphology showed a comparable distribution between sessile and pedunculated types across all 3 groups. Complete resection rates were 88% for HGD, 93% for IMC and 100% for CIS.

### Differences in management based on pathologic diagnoses

Fifty-five patients (24%) were in the IEI group. Our analysis showed statistically significant higher rates of inappropriate early endoscopic follow-up for IMC (odds ratio [OR] 4.09, 95% confidence interval [CI] 1.52-11.5; P=0.01) and CIS (OR 3.70, 95%CI 0.57-29.7; P=0.17) relative to HGD. Intramucosal carcinoma was associated with higher odds of surgical intervention compared to high-grade dysplasia (OR 2.06, 95%CI 0.64–6.66), though this did not reach statistical significance (P=0.237).

### Difference in outcomes for ASI vs. IEI surveillance

Surveillance colonoscopy data were available for 84 patients (53.8%) in the ASI group and 29 (56.9%) in the IEI group (P=0.75). No significant differences between the 2 groups were observed in outcomes at the first surveillance colonoscopy. Approximately half of the surveillance colonoscopies were normal in both groups (45% in ASI and 50% in IEI). Adenomas were detected in 30% of patients in both groups. Advanced adenomas were identified in 7% of the ASI group, whereas none were detected in the IEI group. No cases of CRC were diagnosed in either group at the next surveillance colonoscopy (Table 2).

### Predictors for IEI surveillance

Race, location, endoscopic appearance of lesion, resection type, margins and pathology were statistically significant predictors of IEI by univariate analysis (Table 2). Black race (OR 2.39, 95%CI 1.17-5.03; P=0.02), *en bloc* resection (OR 10.9, 95%CI 3.53-49.0; P<0.001), and IMC (OR 4.09, 95%CI 1.52-11.50; P=0.01) independently predicted greater odds of IEI by binary logistic regression (Fig. 2). Although lesion location and endoscopic appearance reached statistical significance on univariate analysis,

these findings were driven by sparse cell distributions and were not retained in multivariate modeling, given the lack of independent association and limited clinical relevance.

### Discussion

Our study shows that, when compared to HGD, the usage of IMC or CIS in pathology reports after resection of colon adenomas leads to inappropriate endoscopic interval follow-up recommendations for the next surveillance colonoscopy. These findings were statistically significant despite the small sample size. Although a higher rate of referral for surgery was observed, the results did not reach statistical significance, because of the small sample size and the rarity of CIS or IMC reporting. No differences were found in outcomes at the next surveillance colonoscopy for IEI compared to ASI, and no cases of CRC were detected in either group. Although we did not observe any statistically significant differences, the study had sufficient power to be able to detect moderate to large effects, meaning that any true difference was likely to be very small in magnitude. In our study, Black race, *en bloc* resection, and a pathologic diagnosis of IMC were identified as independent predictors of IEI by multivariable analysis.

HGD in colorectal adenomas is a rare diagnosis, with prevalence rates ranging from 0.9-7.9% in existing studies [21,22]. The rarity of reports means that prevalence rates of IMC or CIS in colonic adenomas are unknown. To the best of our knowledge, differences in outcomes among HGD, CIS and IMC in colorectal polyps have not been previously investigated. In eastern countries such as Japan, CIS and IMC are considered cancerous because of their potential to invade the submucosa [23,24]. In contrast, CRC is defined as invasion into or beyond the submucosa in western countries, including the US, where IMC and CIS—being limited to the mucosa—are not believed to have metastatic potential [9,14-16]. This difference has sparked debate. There is concern that endoscopic sampling may not be adequate, and thus cannot exclude deeper invasion, especially if the sampling is done with a biopsy forceps [25]. As a consequence, pathologists often report findings as “at least” CIS or IMC. However, this argument remains true only for superficial biopsy sampling of large masses, which may limit examination of invasion into deeper layers. In the case of complete endoscopic resection via polypectomy with clear margins (>2 mm), the use of CIS or IMC as diagnostic labels offers no added benefit, since there is no evidence supporting their metastatic potential and their management (endoscopic resection) and surveillance strategies (3-year follow up) are similar to those in HGD [17]. This is the first study to support this perspective. No differences in outcomes or interval diagnoses of CRC were observed, even when patients underwent inappropriate early surveillance. A study from The Netherlands conducted at a tertiary referral center for hereditary cancer and population screening identified 14 cases of IMC in patients with Lynch syndrome or IBD-associated dysplasia over a 34-year period [26]. The authors reported a higher prevalence of DNA mismatch repair deficiency (dMMR) in these IMC cases, supporting the relevance of reporting IMC

**Table 1** Summary of patient characteristics by pathologic diagnosis. “Residual” indicates endoscopic evidence of residual polyp as described in the operative note; a designation of “no” signifies that the polyp was not completely removed. “Margin” refers to the assessment of resection margins in the pathology report

Characteristics	Pathologic diagnosis			P-value
	HGD	IMC	CIS	
n	200	28	5	
Age (mean±SD)	64.69±9.98	61.44±10.00	65.20±9.34	0.28
Sex (%)				
Male	121 (60.5)	14 (50.0)	3 (60.0)	0.5
Female	79 (39.5)	14 (50.0)	2 (40.0)	
Ethnicity (%)				
Non-Hispanic	182 (91.0)	24 (85.7)	5 (100.0)	0.34
Hispanic	15 (7.5)	2 (7.1)	0 (0.0)	
Other/unknown	3 (1.5)	2 (7.1)	0 (0.0)	
Race (%)				
White	98 (49.0)	11 (39.3)	2 (40.0)	0.7
Black	80 (40.0)	13 (46.4)	2 (40.0)	
Other/Unknown	22 (11.0)	4 (14.3)	1 (20.0)	
BMI (%)				
18.0-24.9	48 (24.1)	7 (25.0)	2 (40.0)	0.8
25.0-29.9	64 (32.2)	8 (28.6)	1 (20.0)	
30.0-34.9	45 (22.6)	8 (28.6)	0 (0.0)	
≥35	42 (21.1)	5 (17.9)	2 (40.0)	
Indication (%)				
Screening	64 (32.0)	11 (39.3)	1 (20.0)	0.4
Surveillance	36 (18.0)	2 (7.1)	1 (20.0)	
Positive FIT	48 (24.0)	7 (25.0)	3 (60.0)	
Diagnostic	52 (26.0)	8 (28.6)	0 (0.0)	
Location (%)				
Cecum	11 (5.5)	2 (7.1)	0 (0.0)	0.32
Ascending colon	27 (13.5)	1 (3.6)	1 (20.0)	
Transverse colon	25 (12.5)	1 (3.6)	0 (0.0)	
Descending colon	22 (11.0)	1 (3.6)	0 (0.0)	
Rectosigmoid	115 (57.5)	23 (82.1)	4 (80.0)	
Endoscopic appearance (%)				
Sessile	85 (42.5)	14 (50.0)	2 (40.0)	0.23
Pedunculated	100 (50.0)	13 (46.4)	2 (40.0)	
Flat	12 (6.0)	0 (0.0)	0 (0.0)	
Mass	3 (1.5)	1 (3.6)	1 (20.0)	
Size (%)				
<10 mm	40 (20.0)	1 (3.7)	1 (20.0)	0.53
11-20 mm	72 (36.0)	12 (44.4)	2 (40.0)	
21-30 mm	51 (25.5)	9 (33.3)	2 (40.0)	
31-40 mm	25 (12.5)	5 (18.5)	0 (0.0)	
41-50 mm	8 (4.0)	0 (0.0)	0 (0.0)	
≥51 mm	4 (2.0)	0 (0.0)	0 (0.0)	
Resection (%)				
<i>En bloc</i>	137 (72.9)	17 (63.0)	5 (100.0)	0.25
Piecemeal	51 (27.1)	10 (37.0)	0 (0.0)	
Technique (%)				
Hot	164 (82.0)	27 (96.4)	4 (80.0)	0.24
Cold	19 (9.5)	0 (0.0)	1 (20.0)	
Biopsy	17 (8.5)	1 (3.6)	0 (0.0)	
Residual (%)				
No	177 (88.5)	28 (100.0)	5 (100.0)	0.86
Yes	23 (11.5)	0 (0.0)	0 (0.0)	

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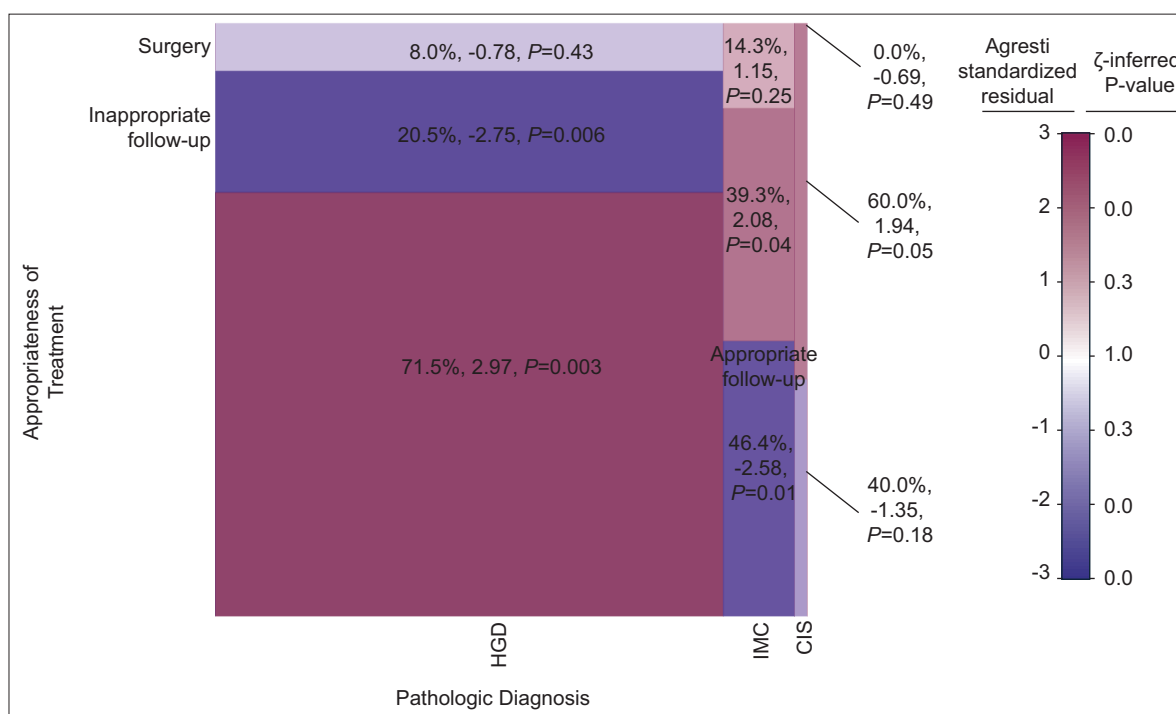
Table 1 (Continued)

Characteristics	Pathologic diagnosis			P-value
	HGD	IMC	CIS	
Margin (%)				
Clear	130 (85.5)	20 (87.0)	4 (80.0)	0.91
Not clear	22 (14.5)	3 (13.0)	1 (20.0)	
Treatment (%)				
Appropriate follow up	143 (71.5)	13 (46.4)	2 (40.0)	0.02
Inappropriate follow up	41 (20.5)	11 (39.3)	3 (60.0)	
Surgery	16 (8.0)	4 (14.3)	0 (0.0)	

†ANOVA and Fisher’s exact tests for continuous and categorical variables, respectively

‡ Hot includes hot snare and hot snare + EMR, cold includes cold snare and cold snare + EMR, biopsy includes FTR and biopsy. Missing values excluded from counts and calculations

HGD, high-grade dysplasia; IMC, intramucosal carcinoma; CIS, carcinoma in situ; SD, standard deviation; BMI, body mass index; FIT, fecal immunochemical test; EMR, endoscopic mucosal resection; FTR, full thickness resection



**Figure 1** Mosaic plot of pathologic diagnosis vs. appropriateness of treatment (area represents observed frequency; color represents Agresti standardized residual and  $\zeta$ -inferred P-value; text represents proportion of diagnosis, Agresti standardized residual, and  $\zeta$ -inferred P-value). An omnibus test shows that there is a statistically significant difference in appropriateness of treatment by pathologic diagnosis ( $P=0.02$ , 2-sided Fisher’s exact test). *Post hoc* tests show that there are statistically significant higher rates of inappropriate follow up for IMC (39.3%,  $P=0.04$ ) and CIS (60.0%,  $P=0.05$ ) relative to HGD (20.5%,  $P=0.006$ ) (proportion of diagnosis,  $\zeta$ -inferred P-value). Also, there is a higher rate of surgery for IMC (14.3%,  $P=0.25$ ) relative to HGD (8.0%,  $P=0.43$ ); however, it is not statistically significant in this study (proportion of diagnosis,  $\zeta$ -inferred  $p$ -value). HGD, high-grade dysplasia; IMC, intramucosal carcinoma; CIS, carcinoma in situ

in high-risk populations. Notably, however, the risk of lymph node metastasis in these patients was low, consistent with prior reports in the literature [9,14-16]. In average-risk patients, such as those included in our study, the prevalence of dMMR is lower, suggesting an even lower risk of lymph node metastasis. These findings further support our conclusion that, in average-risk patients, reporting IMC does not meaningfully impact clinical outcomes.

Labeling these precancerous lesions as carcinoma (IMC or CIS) may cause unnecessary anxiety for patients, particularly in

the era of electronic medical records with patient access [27]. Even after complete endoscopic resection, the use of carcinoma instead of HGD may prompt gastroenterologists to adopt a more cautious approach, leading to recommendations for earlier surveillance colonoscopy, as demonstrated in our study. We hypothesize that the earlier follow up could be influenced by the 1-year follow-up interval recommended for surveillance colonoscopy after surgical resection of CRC [28]. However, this is in conflict with the 3-year follow-up recommendation for HGD with clear resection margins in the USMSTF 2020 guidelines [17].

**Table 2** Summary of patient characteristics by pathologic diagnosis. “Residual” indicates endoscopic evidence of residual polyp as described in the operative note; a designation of “no” signifies that the polyp was not completely removed. “Margin” refers to the assessment of resection margins in the pathology report

Characteristics	Follow up		P-value
	Appropriate	Inappropriate	
n	158	55	
Age (mean±SD)	64.15±9.67	63.77±8.85	0.80
Sex (%)			
Male	98 (62.0)	30 (54.5)	0.34
Female	60 (38.0)	25 (45.5)	
Ethnicity (%)			
Non-Hispanic	146 (92.4)	47 (85.5)	0.14
Hispanic	10 (6.3)	5 (9.1)	
Other/unknown	2 (1.3)	3 (5.5)	
Race (%)			
White	85 (53.8)	19 (34.5)	0.052
Black	56 (35.4)	28 (50.9)	
Other/unknown	17 (10.8)	8 (14.5)	
BMI (%)			
18.0-24.9	39 (24.8)	11 (20.0)	0.72
25.0-29.9	50 (31.8)	18 (32.7)	
30.0-34.9	32 (20.4)	15 (27.3)	
≥ 35	36 (22.9)	11 (20.0)	
Indication (%)			
Screening	54 (34.2)	18 (32.7)	0.98
Surveillance	26 (16.5)	8 (14.5)	
Positive FIT	41 (25.9)	15 (27.3)	
Diagnostic	37 (23.4)	14 (25.5)	
Location (%)			
Cecum	7 (4.4)	3 (5.5)	0.012
Ascending colon	26 (16.5)	0 (0.0)	
Transverse colon	16 (10.1)	8 (14.5)	
Descending colon	17 (10.8)	6 (10.9)	
Rectosigmoid	92 (58.2)	38 (69.1)	
Endoscopic appearance (%)			
Sessile	76 (48.1)	17 (30.9)	0.018
Pedunculated	74 (46.8)	37 (67.3)	
Flat	7 (4.4)	0 (0.0)	
Mass	1 (0.6)	1 (1.8)	
Size (%)			
<10 mm	32 (20.4)	7 (12.7)	0.50
11-20 mm	58 (36.9)	24 (43.6)	
21-30 mm	38 (24.2)	17 (30.9)	
31-40 mm	21 (13.4)	7 (12.7)	
41-50 mm	5 (3.2)	0 (0.0)	
≥51 mm	3 (1.9)	0 (0.0)	
Resection (%)			
<i>En bloc</i>	104 (65.8)	52 (94.5)	<0.001
Piecemeal	54 (34.2)	3 (5.5)	
Technique (%)			
Hot	135 (85.4)	52 (94.5)	0.20
Cold	17 (10.8)	3 (5.5)	
Biopsy	6 (3.8)	0 (0.0)	

(Contd...)

**Table 2 (Continued)**

Characteristics	Follow up		P-value
	Appropriate	Inappropriate	
Residual (%)			
No	151 (95.6)	55 (100)	>0.999
Yes	7 (4.4)	0 (0.0)	
Margin (%)			
Clear	96 (82.1)	55 (100.0)	<0.001
Not clear	21 (17.9)	0 (0.0)	
Surveillance (%)			
Yes	84 (53.8)	29 (56.9)	0.75
No	72 (46.2)	22 (43.1)	
Pathologic finding at first surveillance colonoscopy (%)			
Normal	39 (45.9)	15 (50.0)	0.46
Hyperplastic	11 (12.9)	6 (20.0)	
SSA/P	4 (4.7)	0 (0.0)	
Adenoma	25 (29.4)	9 (30.0)	
Advanced Adenoma	6 (7.1)	0 (0.0)	
Cancer	0 (0.0)	0 (0.0)	
Pathology at index colonoscopy (%)			
HGD	143 (90.5)	41 (74.5)	0.007
IMC	13 (8.2)	11 (20.0)	
CIS	2 (1.3)	3 (5.5)	

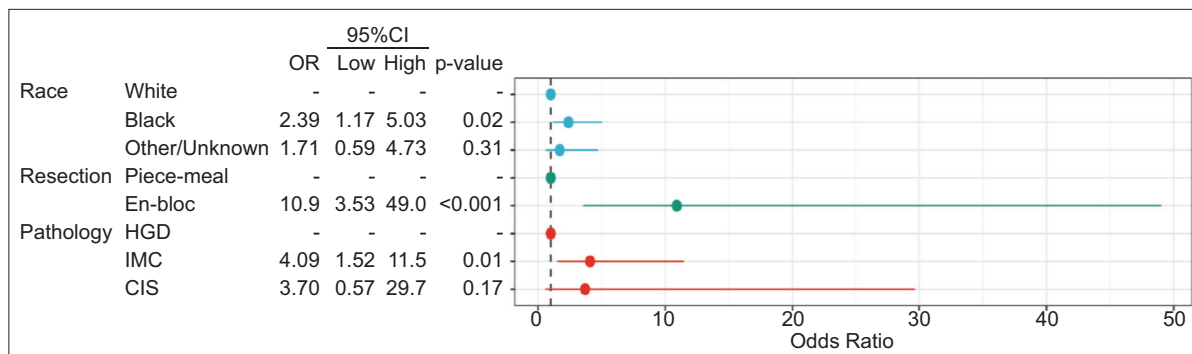
†ANOVA and Fisher’s exact tests for continuous and categorical variables, respectively

‡Hot includes hot snare and hot snare + EMR, cold includes cold snare and cold snare + EMR, biopsy includes FTR and biopsy. Missing values excluded from counts and calculations

SD, standard deviation; BMI, body mass index; FIT, fecal immunochemical test; EMR, endoscopic mucosal resection; FTR, full thickness resection; SSA/P, sessile serrated adenoma/polyp; HGD, high-grade dysplasia; IMC, intramucosal carcinoma; CIS, carcinoma in situ

Although colonoscopy is generally safe, with minimal risk of complications, the cumulative risk for adverse events could increase with more frequent procedures [29]. Additionally, the recent change in the recommended starting age for CRC screening from 50 to 45 years is projected to add approximately 3 million colonoscopies every year in the US, increasing annual screening costs by an estimated \$10 billion [30, 31]. Therefore, to reduce the financial burden on patients and alleviate the strain on national healthcare resources, it is essential to avoid unnecessary colonoscopies and ensure that these services remain accessible to patients with a genuine need for screening.

Most western pathologists are likely to report dysplasia limited to the mucosal layer as HGD rather than IMC or CIS, especially for completely resected colon polyps. Thus, given the rarity of reporting, sample sizes for IMC and CIS are disproportionately small when compared to HGD. In our study, only 5 cases of CIS were included in the study, limiting evaluation for this entity. Black race was noted to be an independent predictor of a



**Figure 2** Binary logistic regression model weakly predicts appropriateness of follow up by race, resection type, and pathology. Larger odds ratio suggests greater odds of inappropriate follow up. Black race vs. white race (OR 2.39, 95%CI 1.17-5.03;  $P=0.02$ ), *en bloc* vs. piecemeal resection (OR 10.9, 95%CI 3.53-49.0;  $P<0.001$ ), and intramucosal carcinoma vs. high-grade dysplasia pathology (OR 4.09, 95%CI 1.52-11.5;  $P=0.01$ ) independently predict greater odds of inappropriate follow up. Initial predictors (race, location, lesion, resection type, margins, pathology) were selected based on statistically significant univariate Fisher's exact tests (see Table 1). Final predictors (race, resection type, pathology) are selected for a parsimonious model ( $k=8$  predictor levels; 96 df to fit intercept plus 15 df per level), maximized ROC AUC, and minimized AIC. Spearman's adjusted  $\rho^2 \leq 0.06$  for all predictors support a linear model. No Incomplete cases.

AIC, Akaike information criterion; OR, odds ratio; CI, confidence interval; HGD, high-grade dysplasia; IMC, intramucosal carcinoma; CIS, carcinoma *in situ*; ROC AUC, receiver operating characteristic area under the curve

recommendation for surveillance at IEI. It could be hypothesized that this finding was due to knowledge regarding existing biases about racial disparities in CRC screening, and the higher risk of CRC in the Black population [32].

*En bloc* resection of colon polyps is known to significantly reduce the risk of polyp recurrence when compared to piecemeal resection [33]. *En bloc* resection allows complete examination of the mucosal layer and enables the pathologist to comment on margins and invasion. Contrastingly, our study showed that *en bloc* resection was an independent predictor of IEI in multivariable analysis, which is counterintuitive in relation to clinical practice [34]. This finding is likely non-causal and reflects confounding by pathologic labeling and management ambiguity, as piecemeal resections typically receive clear guideline-directed short-interval follow up.

Our study had several limitations. The retrospective design introduced potential selection bias, and relied on documentation and diagnostic interpretations that were not standardized for research purposes; this may have influenced our results. In addition, changes in clinical and pathologic practices over time could not be fully accounted for. Cases of HGD were not routinely reviewed by a second pathologist in accordance with institutional practice, which may have affected diagnostic accuracy. While our study was adequately powered for moderate and greater size effects, the study may have lacked the sensitivity to detect small effects, which cannot be excluded. Follow-up data were available for only 53% of patients in the ASI group and 56% in the IEI group, and were limited to the subsequent colonoscopy, preventing the assessment of long-term outcomes. Despite these limitations, in the absence of prior studies evaluating outcomes in this setting, our findings provide a meaningful contribution to the existing literature.

CRC prevention relies on close collaboration between endoscopists and pathologists. Pathologic nomenclature plays a critical role in guiding surveillance colonoscopy intervals following polypectomy. Our study highlights that, in cases of

completely resected colon adenomas, all dysplastic changes confined to the mucosa should be classified as HGD, regardless of intramucosal depth. We found that using terms like IMC or CIS instead of HGD leads to unnecessary colonoscopies and referrals to colorectal surgery for lesions that have been entirely resected. Additionally, our findings show no significant difference in outcomes or interval cancer diagnoses when following the USMSTF guidelines for a 3-year surveillance interval compared to earlier follow up. In conclusion, we recommend using the HGD classification exclusively for mucosa-limited dysplasia in completely resected colon adenomas, while avoiding IMC or CIS terminology. Adopting this evidence-based approach can reduce patient anxiety, minimize diagnostic confusion, and prevent unnecessary endoscopic procedures. Further large-scale studies are needed to validate these findings.

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## Summary Box

### What is already known:

- Colonic adenomas with dysplasia confined to the mucosal layer—referred to as adenomas with high-grade dysplasia—do not metastasize, and endoscopic *en bloc* resection with negative margins is curative
- In rare cases, pathologists may classify these adenomas as intramucosal carcinoma (IMC) or carcinoma *in situ* (CIS), depending on the depth of mucosal invasion
- Labeling mucosal dysplasia as “carcinoma” can lead to unnecessary early surveillance colonoscopies or even referral for surgery

### What the new findings are:

- Despite the small sample size and rarity of reporting, IMC and CIS were significantly associated with higher rates of inappropriately early surveillance colonoscopy
- Black race, *en bloc* resection and a pathologic diagnosis of IMC were identified as independent predictors of inappropriately early surveillance recommendations
- No differences in outcome were observed at next surveillance colonoscopy when comparing appropriate vs. inappropriate surveillance duration, and no interval cancer was noted in either group at first surveillance colonoscopy

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