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# Influence of SCENIC recommendations on terminology used for histopathologic diagnosis of inflammatory bowel disease-associated dysplasia

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## Abstract

### BACKGROUND

Published in 2015, the International Consensus Recommendations on Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients (SCENIC) recommended abandoning the use of diagnostic term “dysplasia-associated lesion or mass (DALM)” for polypoid dysplastic lesions detected in patients with inflammatory bowel disease (IBD). The aim of this study was to investigate whether this recommendation had any influence on diagnostic terminologies used by pathologists in their practice.

### METHODS

We retrospectively reviewed all pathology reports for surveillance colonoscopic biopsies from ulcerative colitis (UC) patients in our institution during 1/2012-12/2014 (pre-SCENIC) and 1/2016-12/2018 (post-SCENIC). These included 1203 biopsies from 901 UC patients during the pre-SCENIC period and 1273 biopsies from 977 UC patients during the post-SCENIC period. Their corresponding endoscopic findings and histopathologic diagnoses were recorded. Clinical indications for total colectomy for UC patients and corresponding histopathologic findings in colectomy specimens were also recorded and compared.

### RESULTS

A total of 347 and 419 polyps/polypoid lesions were identified during the pre-SCENIC and post-SCENIC periods, among which 60 and 104 were dysplastic/adenomatous, respectively. More polypoid dysplastic lesions were simply diagnosed as “adenoma” during the post-SCENIC period in comparison with the

pre-SCENIC period (97.1% vs 65.0%;  $P < 0.001$ ). The number of cases with a comment in pathology reports regarding the distinction between DALM and sporadic adenoma was also significantly decreased during the post-SCENIC period (5.8% vs 38.3%;  $P < 0.001$ ). In addition, the term “dysplasia” was more consistently used for random biopsies during the post-SCENIC period. Furthermore, the terms “sessile serrated adenoma/polyp” (SSA/P) and “serrated epithelial change” (SEC) were more consistently used for polypoid lesions and random biopsies, respectively, during the post-SCENIC period, although these were not specifically addressed in the SCENIC recommendations. The indications for colectomy remained unchanged, however, despite the standardization of diagnostic terminologies.

### CONCLUSION

The SCENIC recommendations relieve pathologists from the burden of distinguishing DALM from sporadic adenoma in IBD patients, which helps the standardization of diagnostic terminologies used by pathologists. The consistent use of the diagnostic terminologies may help reduce potential confusions to clinicians and patients.

**Key Words:** Inflammatory bowel disease; Ulcerative colitis; Dysplasia; Terminology; SCENIC

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**Core Tip:** The Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients recommendations help relieve pathologists from the burden of histologically distinguishing dysplasia-associated lesion or mass from sporadic adenoma in inflammatory bowel disease patients, which is an extremely challenging and stressful differential. This has a significant influence on diagnostic terminologies used by pathologists in their practice.

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## INTRODUCTION

Patients with inflammatory bowel disease (IBD), either ulcerative colitis (UC) or Crohn disease (CD), have an increased risk of developing colorectal cancer (CRC). IBD-associated CRC constitutes 10%-15% of deaths in IBD patients[1]. The risk of developing CRC in UC is similar to that in CD[2,3]. Dysplasia, which is stratified by histopathologic features into low-grade dysplasia (LGD) and high-grade dysplasia (HGD), is currently considered the best marker of CRC risk in IBD. Surveillance colonoscopy therefore is recommended to detect dysplasia for early CRC prevention. Dysplastic foci may be visible under colonoscopy as raised lesions or invisible found on random (non-targeted) biopsies of the colonic mucosa. Invisible dysplasia, especially HGD, is usually an indication of total colectomy.

Raised or polypoid dysplasia in the setting of IBD has been termed “dysplasia-associated lesion or mass (DALM)” in the past, which was believed to be associated with a high risk for CRC development [4,5]. Therefore, a diagnosis of DALM usually meant total colectomy for cancer prevention[5]. However, it is extremely difficult or even impossible for endoscopists and pathologists to distinguish a DALM lesion from a sporadic adenoma, another polypoid precancerous lesion of CRC that is not associated with IBD. Similar to that in the general population, the occurrence of sporadic adenoma in IBD patients also increases with age, but its progression to CRC appears to take much longer. Complete removal of a sporadic adenoma by endoscopic polypectomy is considered an adequate treatment for cancer prevention[6]. In addition, with the advancement in endoscopic technology and increasing use of high-resolution endoscopy, chromoendoscopy, image-enhanced endoscopy and magnifying endoscopy, many invisible dysplastic foci under routine endoscopy in IBD patients now become visible[7], and many of them can be completely removed under endoscopy without the necessity of colectomy. Furthermore, recent studies have shown that cancer risk is not increased if DALM lesions can be completely removed by endoscopy, and thus total colectomy is also unnecessary[8,9]. These changes in practice have greatly reduced the necessity of total colectomy for CRC prevention in IBD patients.

With these new developments, the International Consensus Recommendations on Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients (SCENIC) were published in 2015[10], which addressed two important issues: How surveillance colonoscopy should be performed for dysplasia detection, and how dysplasia should be managed.

According to SCENIC recommendations, endoscopically visible dysplasia can be categorized into polypoid ( $\geq 2.5$  mm, pedunculated or sessile) and non-polypoid (superficially elevated and  $< 2.5$  mm, flat or depressed) lesions. It is also recommended that the terms “DALM”, “adenoma-like” and “non-adenoma-like” be abandoned. The aim of this study was to investigate whether the SCENIC recommendations had any influence on the terminologies used by pathologists to diagnose dysplasia detected during surveillance colonoscopies in IBD patients.

## MATERIALS AND METHODS

### Study groups

We retrospectively reviewed all pathology reports from patients who had clinically established diagnosis of UC and underwent surveillance colonoscopy with biopsy at Ronald Reagan UCLA Medical Center during two periods of time: January 2012 through December 2014 (pre-SCENIC) and January 2016 through December 2018 (post-SCENIC). Patients with CD, indeterminate colitis and first-time diagnosis of UC were excluded. Endoscopic biopsies from UC patients who had already undergone total colectomy were also excluded from the study. A total of 1203 colonoscopic biopsies from 901 UC patients during the pre-SCENIC period (2012-2014) and a total of 1273 biopsies from 977 UC patients during the post-SCENIC period (2016-2018) were reviewed. Their corresponding endoscopic findings (e.g., polyp or other elevated lesions) and histopathologic diagnoses (e.g., adenoma, hyperplastic polyp or others) were recorded. Clinical indications for total colectomy for UC patients and corresponding histopathologic findings in colectomy specimens were also recorded and compared between the pre- and post-SCENIC periods. The study was approved by the Institutional Review Board at UCLA.

### Statistical analysis

Clinicopathologic and outcome findings were compared between the pre- and post-SCENIC groups using the  $\chi^2$  or Fisher exact test (for categorical features). All statistical analyses were performed using the SPSS software.  $P < 0.05$  was considered statistically significant.

## RESULTS

### Polyps and polypoid lesions removed by targeted biopsies/polypectomies

A total of 347 polyps/polypoid lesions were detected and removed among 1203 endoscopic biopsies (28.8%) during 2012-2014 (Table 1). Among these polyps/polypoid lesions, 60 (17.3%) were found to be dysplastic/adenomatous. In pathology reports, 39 of 60 (65.0%) cases were directly diagnosed as “adenoma” ( $n = 36$ ) or “adenomatous change” ( $n = 3$ ). These included 17 cases with multiple adenomatous lesions. Nineteen (31.7%) cases were diagnosed as “dysplasia” (LGD,  $n = 14$ ; polypoid LGD,  $n = 1$ ; LGD with tubulovillous features,  $n = 2$ ; HGD,  $n = 2$ ), of which 9 had multiple dysplastic lesions. One (1.7%) polypoid dysplastic lesion was diagnosed as “DALM”, and another polyp was diagnosed as “combined serrated and low-grade adenomatous features”. A comment on the distinction between sporadic adenoma and DALM was included in pathology reports for 23 (38.3%) of these cases (Table 2). These included 9 of 39 (23.1%) cases diagnosed as “adenoma” or “adenomatous change” and 13 of 19 (68.4%) cases diagnosed as “dysplasia”. Of the cases diagnosed as “adenoma”, sporadic adenoma was favored for 5 (55.6%) cases in the comment, DALM for 2 (22.2%), and indistinguishable for 2 (22.2%). Of the cases diagnosed as “dysplasia”, sporadic adenoma was favored for 4 (30.8%) cases, DALM for 2 (15.4%), and indistinguishable for 7 (53.8%). The single case diagnosed as “DALM” also had a comment to further favor the diagnosis.

As shown in Table 1, a total of 419 polyps/polypoid lesions were identified and removed among 1273 endoscopic biopsies (32.9%) during 2016-2018. Of the 104 (24.8%) polyps/polypoid lesions that were found to be dysplastic/adenomatous, 101 (97.1%) were directly diagnosed as “adenoma”. These included 21 cases with multiple adenomatous lesions. Only 3 (2.9%) polyps was diagnosed as “dysplasia”, which were all diagnosed in 2016. As shown in Table 2, only 6 (5.8%) of these cases had a comment in pathology reports on the distinction between sporadic adenoma and DALM, including 4 cases diagnosed as “adenoma” (all favored sporadic adenoma) and 2 diagnosed as “dysplasia” (both stated as indistinguishable). Except for one case diagnosed in early 2017, all cases with comments were diagnosed in 2016.

Compared to the pre-SCENIC period, more cases were simply diagnosed as adenoma (97.1% vs 65.0%;  $P < 0.001$ ) and much fewer cases had a comment in pathology reports (5.8% vs 38.3%;  $P < 0.001$ ) during the post-SCENIC period. In fact, all polyps or polypoid lesions that showed dysplastic/adenomatous features were simply diagnosed as adenoma since 2017, and none of these cases had a comment in pathology report regarding the distinction between sporadic adenoma and DALM after early 2017.

**Table 1 Histopathologic diagnoses of polyps and polypoid lesions detected during surveillance colonoscopies in ulcerative colitis patients during pre-SCENIC (2012-2014) and post-SCENIC (2016-2018) periods**

Histopathologic diagnosis	Pre-SCENIC (n = 347)	Post-SCENIC (n = 419)
Adenocarcinoma	3	3
TA	32	80
TVA	2	17
VA	0	2
Adenoma with HGD	2	2
LGD	14	1
LGD with focal HGD	0	1
HGD	2	1
Polypoid LGD	1	0
LGD with tubulovillous features	2	0
Adenomatous change/LGD	2	0
Adenomatous change with focal HGD	1	0
DALM	1	0
Combined serrated and low-grade adenomatous features	1	0
IND	14	6
HP	55	63
SSA/P	9	22
TSA	0	1
Hyperplastic change	51	81
Serrated epithelial change	1	0
Inflammatory polyp/pseudopolyp	143	96
Benign lymphoid aggregate	5	17
Well-differentiated NET	0	1
Pneumatosis intestinalis	0	1
Mucosal prolapse	0	2
Collagenous colitis	0	1
Submucosal giant cells	1	0
Atypical epithelial proliferation	0	1
Polypoid normal mucosa	4	20
Branching crypts	1	0

SCENIC: Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients; UC: Ulcerative colitis; TA: Tubular adenoma; TVA: Tubulovillous adenoma; VA: Villous adenoma; LGD: Low-grade dysplasia; HGD: High-grade dysplasia; DALM: Dysplasia-associated lesion or mass; IND: Indefinite for dysplasia; HP: Hyperplastic polyp; SSA/P: Sessile serrated adenoma/polyp; TSA: Traditional serrated adenoma; NET: Neuroendocrine tumor.

### ***Invisible dysplasia on random biopsies***

During 2012-2014, 17 of 1203 (1.4%) cases were diagnosed to have dysplasia on random biopsies (Table 3). Among them, 8 (47.1%) showed multiple foci of or extensive dysplasia. Five (29.4%) cases had a comment in pathology reports. For 2 cases, IBD-associated dysplasia was favored considering the background of chronic colitis and the random nature of the biopsies. One case was diagnosed as “low-grade adenomatous change” and sporadic adenoma was favored in the comment despite the random nature of the biopsy. For the remaining 2 cases, the comment stated that a definitive distinction between IBD-associated dysplasia and sporadic adenoma could not be made based on histologic assessment alone and recommended clinical and endoscopic correlation.

**Table 2 Comparison of comments on histopathologic diagnoses of polypoid adenomatous/dysplastic lesions detected in ulcerative colitis patients during surveillance colonoscopies between pre-SCENIC (2012-2014) and post-SCENIC (2016-2018) periods**

Histopathologic diagnosis	No. of cases (%)	Comment			
		No. of cases	Favor sporadic adenoma	Favor DALM	Cannot distinguish
Pre-SCENIC					
TA	32 (53.3)	6	5		1
TVA	2 (3.3)	0			
TA with focal HGD	2 (3.3)	0			
Adenomatous change/LGD	2 (3.3)	2		1	1
Adenomatous change with focal HGD	1 (1.7)	1		1	
LGD	14 (23.3)	10	4	1	5
Polypoid LGD	1 (1.7)	1			1
LGD with tubulovillous features	2 (3.3)	2		1	1
HGD	2 (3.3)	0			
DALM	1 (1.7)	1		1	
Combined serrated and low-grade adenomatous features	1 (1.7)	0			
Total	60 (100)	23	9	5	9
Post-SCENIC					
TA	80 (76.9)	4	4		
TVA	17 (16.3)	0			
TVA with focal HGD	2 (1.9)	0			
VA	2 (1.9)	0			
LGD	1 (1.0)	1			1
LGD with focal HGD	1 (1.0)	1			1
HGD	1 (1.0)	0			
Total	104 (100)	6	4	0	2

SCENIC: Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients; UC: Ulcerative colitis; DALM: Dysplasia-associated lesion or mass; TA: Tubular adenoma; TVA: Tubulovillous adenoma; VA: Villous adenoma; LGD: Low-grade dysplasia; HGD: High-grade dysplasia.

During 2016-2018, 16 of 1273 (1.3%) cases were diagnosed to have dysplasia on random biopsies, including 9 (56.3%) that showed multiple foci of or extensive dysplasia. Three (18.8%) cases had a comment in pathology report on the nature of dysplasia, including 2 diagnosed in 2016 and one in 2017. IBD-associated dysplasia was considered in the comment for 2 cases. For the other case, diagnosed in 2016, the comment stated that the distinction between IBD-associated dysplasia and sporadic adenoma could not be made reliably on histologic grounds.

There was no significant difference in the frequency of dysplasia diagnosed on random biopsies between the pre- and post-SCENIC periods (1.4% vs 1.3%;  $P > 0.05$ ). However, the terminologies used for the diagnosis appeared to be more consistent during the post-SCENIC period in comparison to the pre-SCENIC period.

#### **SSA/P on targeted biopsies/polypectomies**

During 2012-2014, 9 of 1203 (0.7%) biopsies from UC patients had a diagnosis of SSA/P with variable terms used by pathologists (Table 4). These included "SSA" ( $n = 5$ ), "SSP" ( $n = 1$ ), "SSA/P" ( $n = 2$ ), and "SSA/P with low-grade cytologic dysplasia" ( $n = 1$ ). Three (33.3%) cases, biopsied from "thickened fold", had a comment in pathology reports on the significance of serrated polyps in the setting of IBD. Seven (77.8%) cases had follow-up colonoscopic biopsies ( $n = 5$ ) or surgical resections ( $n = 2$ ). Of the 2 resection cases, one case that showed SSA/P with cytologic dysplasia and multiple synchronous tubular adenomas (TA) on surveillance biopsies still showed adenomas in resection specimen. No HGD or

**Table 3 Histopathologic diagnoses of dysplastic lesions on random endoscopic biopsies from ulcerative colitis patients during pre-SCENIC (2012-2014) and post-SCENIC (2016-2018) periods**

Histopathologic diagnosis	No. of cases	Multiple or extensive	Comment			
			No. of cases	Favor sporadic adenoma	Favor IBD dysplasia	Cannot distinguish
Pre-SCENIC						
LGD	13	5	3		2	1
LGD, villous type	1	1	1			1
Low-grade adenomatous change	1	0	1	1		
Low-grade villous dysplasia	1	1	0			
HGD	1	1	0			
Total	17	8	5			
Post-SCENIC						
LGD	12	7	3		2 <sup>1</sup>	1 <sup>2</sup>
LGD/TA	2	1	0			
HGD	2	1	0			
Total	16	9	3			

<sup>1</sup>Diagnosed in 2016 and 2017.

<sup>2</sup>Diagnosed in 2016.

SCENIC: Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients; UC: Ulcerative colitis; IBD: Inflammatory bowel disease; LGD: Low-grade dysplasia; HGD: High-grade dysplasia; TA: Tubular adenoma.

invasive carcinoma was identified. The other case had resection for prior diagnosed dysplasia and sigmoid stricture. No dysplasia, adenoma or invasive carcinoma was identified in resection specimen for this case. The remaining 5 cases had no dysplasia or adenoma identified in the follow-up biopsies.

During 2016-2018, 22 of 1273 cases (1.7%) from 19 patients were diagnosed as "SSA/P", including one case diagnosed as "SSA" in 2018 and one case diagnosed as "SSA/P with low-grade cytologic dysplasia". None of the cases had a comment in pathology report on the significance of the lesion. Six (27.3%) patients had follow-up data from subsequent colonoscopic biopsies. Adenoma was found in one and SSA/P in 2 patients. No dysplastic lesions were detected in the remaining 3 patients. None of the patients underwent surgical resection.

### **SEC on random biopsies**

During 2012-2014, a total of 49 (4.1%) cases showed serrated colonic mucosa on random biopsies (Table 5), which was termed "hyperplastic change" ( $n = 47$ ) or "SEC" ( $n = 2$ ). The most common locations were the left colon and rectum (71.4%). Synchronous adenoma/dysplasia was found in 9 (18.4%) cases. Five of them had synchronous TA including 2 with multiple TAs. The other 4 cases had synchronous LGD on random biopsies including 2 with multiple foci of LGD. Thirty-five (71.4%) cases had follow-up biopsies. Metachronous adenoma/LGD was found in 7 (20.0%) of these cases including one case with multiple tubulovillous adenomas (TVA) and 3 cases with LGD on random biopsies.

During 2016-2018, a total of 66 (5.2%) cases showed serrated colonic mucosa on random biopsies, which was termed "hyperplastic change" ( $n = 61$ ), "SEC" ( $n = 3$ ), and "SSA/P" ( $n = 2$ ). Similar to that seen during pre-SCENIC period, the left colon and rectum were the most common locations (72.7%). Synchronous adenoma/dysplasia was found in 9 (13.6%) cases. Five of them had synchronous TA, 2 had LGD on random biopsies, and 2 had SSA/P. Thirty-five (53.0%) cases had follow-up biopsies. Metachronous adenoma/dysplasia was found in 10 (28.6%) cases including 2 cases showing LGD on random biopsies.

### **Indications for total colectomies**

Table 6 shows that during 2012-2014, a total of 54 UC patients underwent total colectomies, 40 (74.1%) of which were done for medically refractory colitis ( $n = 34$ ) or nonneoplastic complications ( $n = 6$ ). These patients had no prior history of dysplasia or neoplasia. Histopathologic examination of colectomy specimens showed no dysplasia or neoplasia in 38 (95%) cases. One of the two remaining cases was incidentally found to have multiple foci of well-differentiated (low-grade) neuroendocrine tumor in the

**Table 4 Comparison of Sessile serrated adenoma/polyp diagnosed in ulcerative colitis patients between pre-SCENIC (2012-2014) and post-SCENIC (2016-2018) periods**

	Pre-SCENIC		Post-SCENIC	
	No.	%	No.	%
No. of biopsies/patients	9/9		22/17	
Frequency	9/1203	0.7	22/1273	1.7
Diagnosis				
	SSA/P	3 <sup>1</sup>	21 <sup>1</sup>	95.5
	SSA	5	1	4.5
	SSP	1	0	
Single	9	100	17	77.3
Multiple	0		5	22.7
	Right	4	9	41
	Transverse	1	5	22.7
Location	Left	3	4	18.2
	Rectum	1	2	9.1
	Multiple sites	0	2	9.1
Synchronous adenoma	4 <sup>2</sup>	44.4	4 <sup>3</sup>	21.1
No. of patients with follow-up				
	Biopsy	5	6	
	Resection	2 <sup>4</sup>	0	
Metachronous adenoma	4 <sup>5</sup>	44.4	3 <sup>6</sup>	15.8

<sup>1</sup>One case with low-grade cytologic dysplasia.

<sup>2</sup>Tubular adenoma (TA) = 2, TA with focal high-grade dysplasia = 1, indefinite for dysplasia = 1.

<sup>3</sup>TA = 4.

<sup>4</sup>One case had history of pseudopolyps, dysplasia, and sigmoid stricture. The other case had synchronous multiple TAs/low-grade dysplasia (LGD).

<sup>5</sup>TA/LGD = 3, dysplasia (grade not provided) = 1.

<sup>6</sup>TA = 2, TA and sessile serrated adenoma/polyp = 1.

SCENIC: Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients; SSA: Sessile serrated adenoma; SSP: Sessile serrated polyp; SSA/P: Sessile serrated adenoma/polyp.

rectum that ranged in size from 0.3 cm to 1.0 cm and invaded the lamina propria, muscularis mucosae and focally the superficial submucosa. No lymph node metastasis was identified. The other case was found to have a small TA. Fourteen (25.9%) patients underwent surgeries for adenocarcinoma or dysplasia detected on surveillance colonoscopies. Six (42.9%) cases were found to have invasive adenocarcinoma in resection specimens.

During 2016-2018, 40 patients underwent total colectomies, 28 (70.0%) of which were done for refractory colitis ( $n = 26$ ) or nonneoplastic complications ( $n = 2$ ). These patients did not have a prior history of dysplasia or neoplasia. On resection specimens, focal LGD was incidentally found in one case. There was another case where surveillance biopsy showed a focus indefinite for dysplasia but the resection specimen showed extensive HGD. Twelve (30.0%) patients had colectomies for carcinoma, dysplasia or large adenomas detected on surveillance colonoscopies. Invasive carcinoma was found in resection specimens in 7 (58.3%) cases, among which 2 were poorly differentiated neuroendocrine carcinomas. Two cases with preoperative diagnosis of adenocarcinoma showed no residual carcinoma or dysplasia in resection specimens. One case had a 1.5 cm polyp that was completely removed by endoscopic polypectomy prior to surgery. The other case was treated with neoadjuvant chemotherapy prior to surgery with complete response.

## DISCUSSION

Dysplasia in IBD can be either flat (endoscopically invisible) or elevated (endoscopically visible). Elevated lesions were used to be called "DALMs", which were believed to have a high association with cancer and thus regarded as a strong indication for colectomy[11]. DALMs are a group of heterogeneous



**Table 5 Comparison of serrated epithelial change diagnosed on random endoscopic biopsies from ulcerative colitis patients between pre-SCENIC (2012-2014) and post-SCENIC (2016-2018) periods**

		Pre-SCENIC		Post-SCENIC		
		Hyperplastic change (%)	SEC	Hyperplastic change (%)	SEC	SSA/P
Total		47	2	61	3	2
Location	Right	2 (4.3)	0	5 (8.2)	0	1
	Transverse	2 (4.3)	0	3 (4.9)	0	1
	Left	17 (36.2)	2	14 (23.0)	1	0
	Rectum	16 (34.0)	0	31 (50.8)	0	0
	Multiple sites	10 (21.3)	0	8 (13.1)	2	0
Synchronous adenoma/ dysplasia						
	TA	4 <sup>1</sup> (8.5)	1 <sup>1</sup>	5 (8.2)	0	0
	LGD	4 <sup>2</sup> (8.5)	0	2 (3.3)	0	0
	SSA/P	0	0	1 (1.6)	1	0
No. of cases with follow-up biopsies		33	2	31	3	1
Metachronous dysplasia						
	TVA	1 <sup>1</sup> (3.0)	0	1 (3.2)	0	0
	TA	1 (3.0)	1	6 <sup>1</sup> (19.4)	0	0
	LGD	3 (9.1)	0	2 (6.5)	0	0
	SSA/P	1 (3.0)	0	1 (3.2)	0	0
	IND	0	0	1 (3.2)	0	0

<sup>1</sup>One case had multiple adenomas.

<sup>2</sup>Two cases had multiple foci of LGD.

SCENIC: Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients; SEC: Serrated epithelial change; SSA/P: Sessile serrated adenoma/polyp; TA: Tubular adenoma; TVA: Tubulovillous adenoma; LGD: Low-grade dysplasia; IND: Indefinite for dysplasia.

lesions which can be further divided into adenoma-like and non-adenoma-like based on their endoscopic appearance. Non-adenoma-like DALMs refer to velvety patches, plaques, irregular bumps and nodules, wart-like thickenings, stricturing lesions, and broad-based masses. These lesions are believed to carry a high risk of concurrent malignancy, often representing the surface of an invasive adenocarcinoma and therefore often requiring colectomy[8]. On the other hand, adenoma-like DALMs are well-circumscribed lesions similar to sporadic adenomas endoscopically and pathologically. It has been suggested that adenoma-like DALMs that occur outside or proximal to the areas of mucosa involved by inflammation are considered sporadic in origin and can be managed conservatively by polypectomy. On the contrary, adenoma-like DALMs detected within the area of inflammation may be IBD-associated and thus colectomy and close surveillance may need to be considered. Other features favoring IBD-associated adenoma-like DALMs include young age at diagnosis, long duration of disease, prominent villous architecture, a mixture of normal and dysplastic epithelia at the surface of polyp, "bottom-up" dysplasia, increased inflammation in polyp, presence of stalk dysplasia, and a high frequency of *p53* and a low frequency of *KRAS* mutations[12-15]. However, none of these features has proven to be specific despite the great efforts made by pathologists in the distinction between IBD-associated adenoma-like DALMs and sporadic adenomas.

In 2015, the SCENIC recommendations were published, which incorporated the latest understanding on surveillance and management of dysplasia in IBD[10]. According to this consensus, dysplastic lesions can be simply classified as endoscopically visible and invisible. Visible dysplasia, by definition, is histopathologically proven dysplasia on a targeted biopsy of a concerning area recognized on colonoscopic examination. Invisible dysplasia is histopathologically proven dysplasia on a random biopsy from a visually unremarkable colonic mucosa[10]. For endoscopically visible lesions, the determination of endoscopic resectability, rather than the distinction between adenoma-like and non-adenoma-like or between IBD-associated dysplasia and sporadic adenoma, becomes important according to the consensus recommendations. Therefore, the term "DALM" becomes no longer useful and should be abandoned. For endoscopically visible and resectable lesions, either polypoid or non-polypoid,

**Table 6 Indications for total colectomies and postoperative findings for ulcerative colitis patients during pre-SCENIC (2012-2014) and post-SCENIC (2016-2018) periods**

	No. of cases (%)	Preoperative biopsy/polypectomy (No. of cases)	Postoperative findings (No. of cases)
Pre-SCENIC			
Total	54		
Refractory UC	34 (63.0)	No dysplasia/adenoma or malignancy (34)	Incidental well-differentiated (low-grade) NET (1); TA (1); no dysplasia/adenoma or malignancy (32)
Complications	6 (11.1)	Perforation (2); fistula (1); stricture (1); volvulus (1); obstruction (1) <sup>1</sup>	No dysplasia/adenoma or malignancy (6)
Dysplasia/malignancy	14 (25.9)	Invasive adenocarcinoma (4.5 cm mass lesion), a separate focus of LGD	pT4a pN2b adenocarcinoma, a separate focus of HGD
		Invasive adenocarcinoma (6.3 cm mass), a separate focus of LGD	pT3 pN0 adenocarcinoma
		At least HGD (2.6 cm polypoid lesion)	pT1 pN1a adenocarcinoma (2 foci)
		At least HGD (2.0 cm polypoid lesion)	pT1 pN1a adenocarcinoma (2 foci), separate foci of HGD
		Dysplasia (3.6 cm mass)	pT2 pN1b mucinous adenocarcinoma
		HGD (3.0 cm polypoid lesion), also separate foci of LGD	HGD
		Multiple TAs and foci of LGD, one TA with HGD, one SSA/P with low-grade cytologic dysplasia (0.2-1.5 cm sessile polyps)	Multiple TAs and foci of LGD
		LGD (1.0 cm lesion)	pT1 pN0 mucinous adenocarcinoma arising from extensive LGD
		LGD with tubulovillous features (6.5 cm mucosal plaque)	LGD
		LGD (4.6 cm polypoid lesion)	LGD
		Dysplasia (outside diagnosis)	LGD
		LGD (focal on a random biopsy)	No residual dysplasia or carcinoma
		Extensive LGD	Extensive LGD
		Multiple foci of LGD	Focal LGD
Post-SCENIC			
Total	40		
Refractory UC	26 (65.0)	No dysplasia/adenoma or malignancy (26)	Focal LGD (1); no dysplasia/adenoma or malignancy (25)
Complications	2 (5.0)	Perforation (1); GI bleeding (1) <sup>2</sup>	Extensive HGD (1) <sup>3</sup> ; no dysplasia/adenoma or malignancy (1)
Dysplasia/malignancy	12 (30.0)	Invasive adenocarcinoma (4.1 cm mass)	pT4a pN1a poorly differentiated NEC
		Invasive adenocarcinoma (1.5 cm mass)	pT3 pN1a adenocarcinoma, separate foci of LGD
		Invasive adenocarcinoma (5.5 polypoid mass), a separate focus of LGD	pT3 pN1a poorly differentiated NEC
		Invasive adenocarcinoma with mucinous features arising in a polypoid lesion with serrated/villiform dysplasia (1.5 cm polyp)	No residual carcinoma or dysplasia
		Invasive adenocarcinoma (2.8 cm mass)	No residual carcinoma or dysplasia (s/p neoadjuvant chemotherapy)
		Atypical cells concerning for adenocarcinoma (13.0 cm mass)	pT4b pN0 mucinous adenocarcinoma
		At least HGD (2.5 cm mass)	pT1 pN0 adenocarcinoma with signet-ring cell features (3 foci)

Extensive HGD (3.5 cm flat induration)	pT2 pN0 adenocarcinoma (3 foci)
TVA with focal HGD (6.1 cm mass)	pT2 pN0 adenocarcinoma
Villous adenoma (2.0 cm sessile polyp)	No residual adenoma or carcinoma
Multifocal LGD, one TA	Focal LGD and HGD
LGD with tubulovillous architecture (12 cm polypoid lesion), a separate focus of LGD, multiple TVAs	Villous adenoma

<sup>1</sup>Surveillance colonoscopy found a small polypoid area in the sigmoid colon that caused partial obstruction. Biopsy showed features of sessile serrated adenoma/polyp without cytologic dysplasia. No dysplasia or carcinoma was found on resection specimen.

<sup>2</sup>Surveillance biopsy showed indefinite for dysplasia, resection specimen identified extensive high-grade dysplasia.

SCENIC: Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients; UC: Ulcerative colitis; SSA/P: Sessile serrated adenoma/polyp; NET: Neuroendocrine tumor; TA: Tubular adenoma; TVA: Tubulovillous adenoma; LGD: Low-grade dysplasia; HGD: High-grade dysplasia; IND: Indefinite for dysplasia; NEC: Neuroendocrine carcinoma.

complete endoscopic polypectomy or excision followed by continued surveillance is a sufficient treatment, though the borders of non-polypoid lesions may be difficult to delineate and complete excision can be technically challenging. For patients with endoscopically invisible dysplasia, referral to an experienced IBD specialist with further examination using chromoendoscopy with high-definition colonoscopy is suggested[10,16,17]. If dysplasia is still invisible, management will depend on the grade of dysplasia. While the SCENIC consensus provides recommendations for surveillance and management of dysplasia in IBD patients, no specific suggestions are made on diagnostic terminologies that pathologists should use when reporting dysplastic lesions in IBD patients.

We were curious about whether the SCENIC recommendations had any influence on the terminologies used by pathologists in their reports for the diagnosis of dysplastic/adenomatous lesions detected in IBD patients. According to our single institutional experience, the diagnostic terms used by pathologists were more uniform and consistent in the post-SCENIC period. Specifically, more polypoid dysplastic lesions were directly diagnosed as adenomas (with or without HGD) in the post-SCENIC period (97.1%) in comparison to the pre-SCENIC period (65.0%). In the pre-SCENIC period, approximately one-third of polypoid dysplastic lesions were diagnosed as “LGD” or “HGD”, which could potentially be confused with invisible dysplasia diagnosed on random biopsies. These diagnostic terms have never been used again by pathologists in our institution for targeted biopsies or polypectomies on visible lesions after 2016. It is interesting to note that our pathologists made much less efforts to attempt to distinguish adenoma-like DALM from sporadic adenoma in their practice in the post-SCENIC period. This is evidenced by a dramatic reduction in the number of pathology reports that included a diagnostic comment on the distinction between sporadic adenoma and DALM. In fact, the few cases that had a comment in the post-SCENIC period were all diagnosed in 2016, with only one in early 2017. None of the cases diagnosed after early 2017 carried a diagnostic comment. These changes in practice indicate that pathologists were much less struggling once the stress of distinguishing IBD-associated dysplasia from sporadic adenoma was relieved. It is also interesting to note that in the pre-SCENIC period, only one of 60 (1.7%) polypoid dysplastic lesions was directly diagnosed as “DALM” and only 5 of 23 (21.7%) cases with a comment were favored to be “DALM”, further indicating how cautious the pathologists were in making such a diagnosis given its potential clinical consequence.

For endoscopically invisible dysplasia, histopathologic interpretation of random surveillance biopsies plays an essential role in clinical management. Current recommendation for invisible HGD is colectomy given the high risk of synchronous and metachronous carcinoma[18]. For endoscopically invisible LGD, the management is controversial. The American Society for Gastrointestinal Endoscopy recommended colectomy for multifocal LGD but an individualized approach for unifocal LGD[19]. We had a total of 94 colectomies for UC patients during the pre- and post-SCENIC periods. The majority (72.3%) of the surgeries were performed for medically refractory disease and nonneoplastic complications. The rest of patients (27.7%) had resections for carcinoma, HGD, multifocal LGD, and unifocal LGD diagnosed on surveillance biopsies. There were 4 patients who underwent colectomies for unifocal LGD, all of which occurred during the pre-SCENIC period. Three cases had a polyp/mass detected during surveillance endoscopy, which ranged in size from 1.0 cm to 6.5 cm. Only one case had resection based on histopathologic diagnosis of unifocal LGD on a random surveillance biopsy.

Colorectal serrated polyps, which include hyperplastic polyp, SSA/P and traditional serrated adenoma, have been implicated in the pathogenesis in a subset of CRC. SSA/P in general population has been widely studied[20] and the serrated neoplasia pathway has been thought to be responsible for at least 20% of sporadic CRC[21,22]. These polyps are distinct from conventional adenomas as they frequently harbor *BRAF* mutations and show CpG island methylation. There is evidence, though limited, to support the notion that the clinicopathologic and molecular characteristics of SSA/P found in IBD patients are similar to those in general population[23-25]. Similar to conventional adenomas, these serrated lesions are endoscopically detectable as polyps and thus can be easily removed by

polypectomy. No correlation of occurrence of these lesions with the background inflammation has been reported[25,26]. The changes in our pathology reports also reflected this recognition. During 2012-2014, before SCENIC consensus, variable diagnostic terms had been used including SSA, SSP and SSA/P. A diagnosis comment was included in 1/3 of pathology reports on the nature of the lesion. Since 2016, however, the term SSA/P was consistently used, with no further comment.

SEC, previously called hyperplastic change, is the currently preferred term to describe mucosal changes similar to SSA/P or hyperplastic polyp on biopsies from non-polypoid colonic mucosa from IBD patients. Histologically, it is recognized by distorted architecture but lacks typical features of cytologic dysplasia. It is typically found on random biopsies during surveillance colonoscopy and characterized by serrated crypt architecture, usually involving the upper half of the crypt, and without cytologic features of dysplasia[27]. When endoscopically visible, SEC is typically flat or shows nodular mucosa without a discrete polypoid configuration[28]. Whether SEC carries a risk of progression to dysplasia and CRC is currently unknown, but several studies have suggested that the finding of SEC in IBD patients may be associated with higher rates of colonic synchronous and metachronous neoplasia [27,29,30]. Our limited data also showed a high association of SEC with synchronous and metachronous neoplasia in UC patients. Specifically, of the 81 patients who had a SEC diagnosis, 38 (46.9%) had synchronous or metachronous adenomas. There was no significant difference between the pre-SCENIC and post-SCENIC periods. Further controlled studies are needed to determine whether SEC is indeed a preneoplastic marker in IBD patients.

There are a couple of limitations in this retrospective study. First, this is a single institutional study. Our experience might not be the same as that in other institutions. Second, all data were collected from previous pathology reports signed by different pathologists. It is understandable that different pathologists might have used different diagnostic criteria for various entities and might have different thresholds for the diagnosis of dysplasia even though they were practicing in the same institution. Nonetheless, these limitations did not appear to affect the conclusions of the study.

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## CONCLUSION

Although the SCENIC recommendations were aimed to address management issues, they had a significant impact on the terminologies pathologists used in their practice based on our institutional experience. Specifically, the recommendations relieved pathologists from the burden of distinguishing “DALM” from sporadic adenoma in IBD patients, which is an extremely challenging and stressful differential. Currently, all polypoid or visible dysplastic lesions are simply diagnosed as “adenoma” in our institution, irrespective of whether or not they are IBD-associated because of the same management approaches. The term “dysplasia” is reserved only for invisible lesions found in random biopsies. The consistent use of the diagnostic terminologies may help reduce potential confusions to clinicians and patients.

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## FOOTNOTES

**Author contributions:** Wang HL designed the research, supervised data analysis and manuscript preparation; Li Y collected and analyzed the data, and wrote the manuscript.

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