REVIEW ARTICLE

The colonoscopist's guide to the vocabulary of colorectal neoplasia: histology, morphology, and management

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Prevention of colorectal cancer by colonoscopy requires an effective and safe insertion technique, a high level of detection of pre-cancerous lesions, and skillful use of curative endoscopic resection techniques. Lesion detection, characterization, use of appropriate resection methods, prediction of cancer at colonoscopy, and management of malignant polyps all depend on an accurate and complete understanding of an extensive vocabulary describing the histology and morphology of neoplastic colorectal lesions. Incomplete understanding of vocabulary terms can lead to management errors. We provide a colonoscopist's perspective on the vocabulary of colorectal neoplasia and discuss the interaction of specific terms with management decisions.

Nearly 60% of the eligible U.S. population report being up to date with colorectal cancer screening, with colonoscopy the most commonly used screening test.[1] Many gastroenterologists spend more time performing colonoscopy than any other professional activity. One would expect gastroenterologists to be expert in all aspects of the vocabulary of colorectal neoplasia, including histologic and morphologic classifications of polypoid and flat lesions.

However, speaking to groups of gastroenterologists and other endoscopists, the responses to fundamental questions about colorectal neoplasia are often surprising. For example: How reliable is a pathologist's designation of dysplasia grade in a conventional adenoma? Why is the term "dysplastic adenoma" redundant? Why should the term "intramucosal adenocarcinoma" not be used in pathology reports? What is the histologic difference between a hyperplastic polyp (HP) and a sessile serrated polyp/adenoma? What are the implications of granular versus non-granular morphology in a lateral-spreading tumor? What is the histologic definition of colon cancer?

The answers to these and similar questions provide colonoscopists with critical insights into the limitations of pathology, the proper responses to pathologic interpretations of colon polyps, and in many cases to optimal endoscopic, clinical, or surgical management. A detailed understanding of the implications of both endoscopic appearances and histology is critical in guiding the colonoscopist. The modern expert colonoscopist is able to use electronic chromoendoscopy techniques and established classification schemes to predict lesion histology. Thus, an expert colonoscopist is able to differentiate between a serrated and adenomatous polyp, and between a deeply invasive cancer versus superficial colorectal neoplasia. This review provides a clinically oriented framework to the vocabulary surrounding the main classes of colorectal lesions, particularly the conventional adenomas and serrated lesions. The implications of this vocabulary on management and follow-up are stressed, including how the endoscopic assessment of histology and morphology direct the selection of specific therapies such as EMR, endoscopic submucosal dissection (ESD), and surgical resection.

What are EMR and ESD?

EMR refers to submucosal fluid injection followed by en bloc or piecemeal snare resection. EMR is easier to perform than ESD, requires less training, has a much lower risk of perforation, and a lower need for hospitalization after resection. EMR may be technically quite difficult when lesions are very large, very flat, in a technically challenging position, or when they are accompanied by submucosal fibrosis. Both EMR and ESD have substantial risks of delayed post-polypectomy hemorrhage. For these reasons, many patients with colorectal lesions that are benign and removable by EMR are sent directly to surgery in the United States and Europe,[2,3] even though surgery results in higher costs, morbidity, and mortality than EMR.[4-6]

Abbreviations: ESD, endoscopic submucosal dissection; HP, hyperplastic polyp; JNET, Japan NBI Expert Team; LST, lateral-spreading tumor; MM, muscularis mucosa; NICE, Narrow-band Imaging International Colorectal Endoscopic classification; SSP, sessile serrated polyp; TSA, traditional serrated adenomas; SSA/P, sessile serrated adenoma/polyp.

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ESD was developed in Japan to treat early gastric cancer. ESD has been extended to the colon, where it has been used successfully by Japanese experts[7-9] and increasingly by western experts.[10-12] The technique involves submucosal injection, but ESD does not use snare resection. Specialized endoscopic needle-like knives are used to create a circumferential incision through the mucosa around the lesion, followed by dissection through the submucosa under the lesion. The goal of ESD is en bloc resection in all cases, and ESD is much more likely than EMR to achieve this result.[13] The en bloc tissue specimen is pinned before fixation to provide proper orientation for pathologic assessment of the deep and lateral resection margins. Whether ESD should be used more extensively in the West is controversial. Given the advantages of EMR relative to ESD noted above, which patients and how many patients really benefit from ESD compared with EMR is a critical issue that is discussed in detail below.

The colonoscopist's vocabulary of colorectal cancer

Because the colon has no mucosal lymphatics, colon cancer is defined in western countries as invasion of dysplastic cells into the submucosa. It follows that any neoplastic lesion that is confined to the mucosa, including epithelium, lamina propria, and muscularis mucosa, must be considered pre-cancerous or non-invasive, irrespective of its dysplastic or cytologic appearance, and is best named as low- or high-grade dysplasia. Some pathologists still use terms such as "carcinoma in situ" and "intramucosal adenocarcinoma" to describe lesions involving severe dysplastic changes confined to the epithelium or lamina propria, respectively. However, these terms are often misinterpreted by patients, referring physicians, and sometimes by colonoscopists, as cancer because they include the word "carcinoma." This confusion can result in unnecessary surgery or excessive follow-up for a lesion that is benign by definition. Such lesions have no lymph node or distant metastatic potential because they lack submucosal invasion, and complete endoscopic resection is uniformly curative.[14] Current U.S. National Comprehensive Cancer Network guidelines specifically state, "A malignant polyp is defined as one with cancer invading through the muscularis mucosa and into the submucosa (T1). Tis is not considered a 'malignant polyp'" (https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf). We recommend that colonoscopists meet with their pathologists to reach consensus regarding optimal terminology, and that colonoscopists take the position that pathologists report "high-grade dysplasia" and not use the terms "intramucosal carcinoma" or "carcinoma in situ," in order to reduce the potential for clinical management errors (Table 1). Western colonoscopists may also be confused because Japanese pathologists and gastroenterologists commonly use the term "intramucosal carcinoma" and count it as cancer. This difference is related to cultural and economic issues, whereas no clinical difference is present, ie, endoscopy is still considered completely adequate treatment for such lesions in Japan. We recommend that, in western countries, the terms "carcinoma in situ" and "intramucosal carcinoma" be abandoned because they may lead to incorrect patient management. Terminology should serve patients and physicians by optimizing rather than confusing management, and hence the term cancer is reserved (in the colorectum) in western countries exclusively for submucosal invasion.

TABLE 1. Pathology terms we could do without

Confusing term	Better term
Carcinoma in situ, intramucosal adenocarcinoma	High-grade dysplasia
Sessile serrated adenoma, serrated adenoma	Sessile serrated polyp

What is superficial versus deep submucosal cancer?

When submucosal cancer is present in a pedunculated polyp, endoscopy is usually regarded as an adequate treatment when 3 histologic factors, namely cancer at the resection margin, lympho-vascular invasion, and poor differentiation, are absent.[13] When invasive cancer is present in a flat (ie, non-polypoid) or sessile lesion, the depth of invasion below the muscularis mucosa (MM) should be measured by the pathologist when technically feasible. If the depth is <1000 μm, the submucosal cancer is classified as "superficial." If the depth of invasion is >1000 μm, the cancer demonstrates "deep submucosal invasion." There are elements of subjectivity with this measurement because the MM layer may be disrupted or not visible. Reliable measurement of the depth of invasion is generally considered to require en bloc resection of the lesion by conventional snare techniques for smaller lesions and either en bloc EMR or ESD for lesions >10 to 20 mm. Pinning the lesion to allow proper orientation for histologic sectioning is important.[12,13] When a superficial submucosal cancer does not present lympho-vascular invasion or poor differentiation after an en bloc resection, endoscopic treatment may be considered as adequate because of a very low risk of lymph node metastasis. In contrast, the risk of lymph node metastasis increases substantially when deep submucosal invasion is present.

When deep submucosal invasion is predicted by endoscopic features,[15] it is preferable to avoid endoscopic resection and proceed to surgery. This prevents the risk of endoscopic adverse events, and endoscopic resection followed by pathology demonstrating deep submucosal invasion will result in surgery in any case. If superficial