

Melvin Schapiro, M.D., Series Editor

Flat Polyps: Endoscopic Detection and Treatment



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Colonoscopy offers a method of screening for and prevention of colorectal cancer. Unfortunately, interval cancers still occur after negative screening colonoscopy suggesting that some pre-cancerous lesions may be missed. Flat and serrated polyps are a particular challenge to detect and may explain why some of these cancers occur. Detection of these subtle lesions requires recognition of their existence, training in their detection, careful inspection technique and adequate bowel preparation. Once a large, flat or otherwise complicated polyp is detected, endoscopic methods exist that offer an alternative to surgery. When performed by appropriately trained endoscopists in carefully selected patients, endoscopic resection can reduce the risk and morbidity of resection. In this review we define the types of difficult to detect polyps, methods to increase their detection, and describe available endoscopic resection techniques.

INTRODUCTION

Colorectal cancer remains third in new cancer diagnoses and cause of cancer related death.¹ In addition to colorectal cancer (CRC) screening, colonoscopy also offers cancer prevention by allowing the removal of adenomatous polyps. Despite this benefit, the degree of risk reduction offered by colonoscopy for right-sided CRC has recently been questioned.²

Colorectal cancers develop from adenomatous polyps. Effective colorectal cancer prevention relies

on early identification and removal of these lesions at their pre-malignant stage. Unfortunately, colonoscopy is imperfect and interval cancers occur in up to 6% of patients after screening colonoscopy.³ There are many potential reasons why interval cancers occur however most agree that missed pre-cancerous polyps play an important role. Some of the most subtle and difficult polyps to detect are the flat and serrated polyps, making them a likely culprit for interval cancer. This is particularly true in the right colon where the bowel preparation is often less than ideal.

Once a large flat or serrated polyp is detected, the next challenge is removal. This is especially true in the right colon where positioning can be a difficult. In the past these patients were routinely sent for surgery, however endoscopic methods of resection

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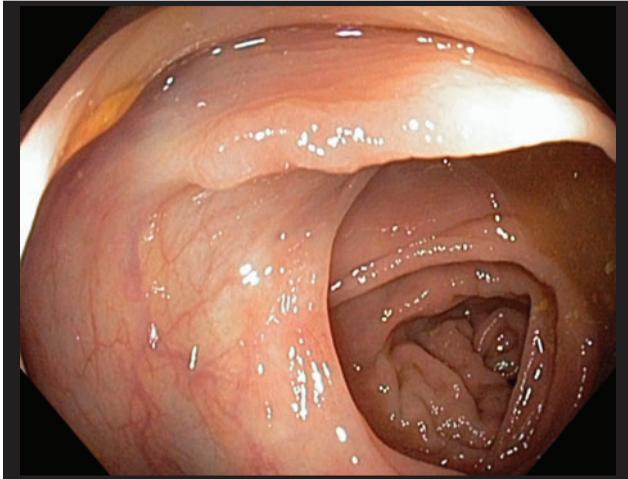


Figure 1. Subtle large flat adenoma

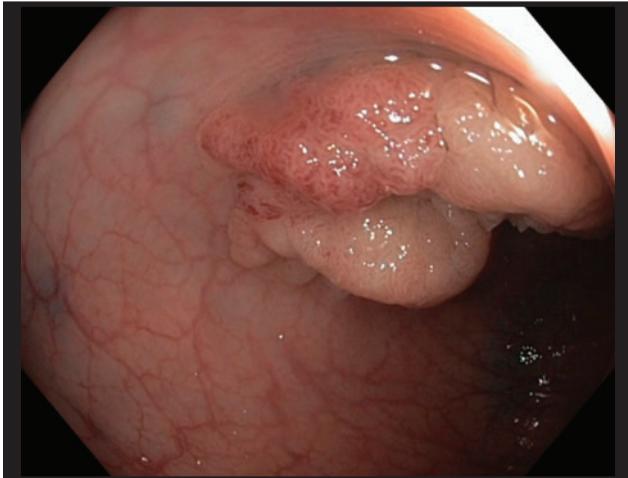


Figure 2: Laterally spreading adenoma, granular type



Figure 3. Flat serrated adenoma covered by adherent mucous cap.

have eliminated the need for surgery for many patients. When done by experienced hands, in carefully selected patients, the risks of endoscopic mucosal resection are only modestly higher than for routine polypectomy.

TYPES OF SUBTLE NEOPLASIA Flat Adenomas

The term flat is used to describe a colon lesion measuring less than 2 cm in size that is elevated less than 2.5mm above the surrounding normal colonic mucosa (figure 1). Flat lesions larger than 2cm are termed “laterally spreading” lesions. Laterally spreading lesions are further sub-divided based on their appearance as either granular (having a nodular appearance, or cluster of sessile lesions) or non-granular (figure 2). As a flat lesion becomes more locally invasive, it penetrates deeper into the colonic wall, becoming a depressed lesion. Depressed lesions have a base that is lower than the normal surrounding mucosa, indicating a higher degree of invasion and dysplasia.

Serrated Polyps

Serrated polyps are now recognized as part of an alternative pathway to colorectal cancer. Unlike the traditional adenoma to carcinoma sequence, colorectal cancers with high levels of microsatellite instability are thought to have developed through a process of CpG island methylation. This process occurs most often in serrated polyps exhibiting BRAF mutations.⁴ Serrated polyps are variants of hyperplastic polyps. They are often flat, located in the right colon and are often covered by an adherent mucous cap, adding to the challenge in their detection (figure 3).

IMPROVING DETECTION Recognition

The first step in improving detection of subtle colorectal lesions is recognizing they exist. Flat and depressed adenomas, collectively referred to as non-polypoid neoplasia, were first described in the colon in the Japanese population over 25 years ago.⁵ Since then, several prospective studies have proven the existence of non-polypoid neoplasia worldwide.

The prevalence of non-polypoid neoplasia in the United States was first described in a landmark study of Veterans Administration (VA) patients. In this study, non-polypoid lesions were found in 9.4% of patients, representing 15% of all polyps detected. Despite their

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small numbers, these non-polypoid lesions accounted for 54% of superficial carcinomas suggesting they are more likely to harbor advanced pathology.⁶ Later studies have resulted in similar findings with approximately 10% of adenomas described as flat.⁷ A tandem colonoscopy study found that up to 32% of flat polyps and 42% of flat adenomas were missed suggesting their true prevalence is likely under-reported.⁸

Despite several studies finding a higher prevalence of advanced pathology in non-polypoid lesions, the US National Polyp Study found the opposite. Flat adenomas in this study were no more likely to contain high-grade dysplasia than their sessile or pedunculated counterparts. Unlike flat lesions, however, truly depressed lesions were found to carry an increased risk for advanced pathology.⁹

Though we are beginning to appreciate the role of serrated polyps in colorectal cancer, their true prevalence is unknown. Confusing nomenclature and lack of agreement in diagnostic criteria have resulted in underreporting of serrated polyps by endoscopists and pathologists alike. What literature does exist suggests that up to 6-10% of patients undergoing screening colonoscopy may have a serrated polyp.¹⁰

This diagnostic challenge has led many gastroenterologists to argue that large hyperplastic polyps, particularly in the right colon, should be treated as neoplastic. Though not currently included in our multi-society surveillance interval guidelines, large hyperplastic polyps should be considered when determining a patient's lifetime risk of colorectal cancer and need for surveillance. In our practice, large hyperplastic polyps prompt surveillance intervals that mirror those assigned to similar size adenomatous polyps. More studies are needed to address this issue and to determine the true impact these polyps have on colorectal cancer risk.

Subtle Clues to Detection

It is often only a subtle clue that will suggest the presence of a flat polyp. Among these are subtle color differences compared to the surrounding mucosa such as an area that appears slightly more red or pale. Spontaneous mucosal hemorrhage or easy friability often indicate presence of neoplasia, however these findings are easy to misinterpret as minor mucosal trauma caused by the colonoscope. Deformity of the colon wall, in particular of the folds, and absence of vascularity in the

region of a flat polyp are other subtle clues. In the right colon, serrated polyps can be particularly challenging to detect as they are often covered with an adherent mucous cap that requires aggressive rinsing to reveal the underlying polyp. Residual stool and adherent bile seen with inadequate bowel preparation can easily mask these subtle clues hindering detection.

Bowel Preparation

The importance of excellent bowel preparation in the detection of non-polypoid neoplasia cannot be emphasized enough. A retrospective study that examined the outcomes in 5000 patients after screening colonoscopy highlights this importance. Of the 17 interval cancers that occurred in these patients, 6 had screening colonoscopies that were incomplete due to poor prep and another 4 had a lesion seen but not recognized as malignant. Considerably lower flat polyp detection was also seen in those who had inadequate prep (9%) compared to those with adequate prep (28%).¹¹

Many bowel purgatives exist. Patients should be instructed on the importance of a good bowel preparation and encouraged to follow the preparation instructions provided. Our practice has adopted a split bowel prep regimen that has shown to provide better overall bowel preparation, but more importantly, better preparation of the right colon.

Inspection Techniques

Adenoma detection is a validated predictor of interval colorectal cancer¹² that is strongly influenced by the performing endoscopist.¹³ Despite this, wide variability exists between endoscopists in this important measure. When high adenoma detectors have been studied formally, certain behaviors are observed. Compared to low detectors, high adenoma detectors spend more time on inspection of proximal surfaces, used irrigation more often to cleanse segments of poorly prepped colon mucosa, distended the colon more during inspection and used tip deflection to look behind colonic folds.¹⁴ These techniques are simple to teach and when incorporated into routine practice result in increased adenoma detection.

In our prospective study, we introduced an endoscopist training module that focused on recognizing the clues of subtle polyps and on the techniques associated with high adenoma detectors. In doing so

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we found an increase in overall adenoma detection from 36% to 47% in those who received training.¹⁵ Our results highlight the importance of training to improve recognition and detection of subtle lesions. In the age of quality measure reporting, patients and providers will have increasing access to the adenoma detection rates of endoscopists. This access will provide physicians with the ability to refer patients to gastroenterologists who offer the highest level of colorectal cancer risk reduction.

Treatment

Most polyps, including those that are flat, are less than 10mm and can be managed easily during routine colonoscopy. In contrast, large, flat polyps often require specialized techniques, which require additional devices, skill and time. As a result, patients with very large flat polyps have historically been referred for surgical resection. Though complete cure can be ensured with surgical resection, it also comes with significant cost, increased risk of morbidity, and in rare cases mortality, for what are most often benign lesions. Endoscopic mucosal resection (EMR) and endoscopic sub-mucosal dissection (ESD) are terms used to describe a variety of devices and techniques used to resect large polyps, and in some cases, early colorectal cancers.

The technique of EMR was first described for flexible colonoscopy in 1973 and has been practiced widely in regions, such as Japan, with a high prevalence of large, flat lesions. As large, flat lesions have become increasingly recognized worldwide, EMR has become more widely adopted. Several tools exist that allow safe removal of large lesions that are limited to the superficial mucosal layer. These include lift and snare, cap-assisted and ligation-assisted techniques, each with the goal to remove all neoplastic tissue down to the sub-mucosal layer.¹⁶

Endoscopic mucosal resection has proven a safe alternative to surgery in experienced hands. Major complications such as bleeding and perforation are infrequent, occurring in 0.5 to 6% of cases depending on the series.¹⁷ The risk of bleeding is directly related to the size of the polyp with those larger than 3 cm conferring the greatest risk.^{18,19} This knowledge allows endoscopists to apply endoscopic closure devices as prophylaxis against bleeding.

One major limitation to EMR is that large lesions (>20mm) require piece-meal resection, which prohibits

accurate pathologic margin assessment. Advanced imaging modalities such as high definition white light imaging, dye-based or virtual chromoendoscopy, and confocal endomicroscopy can aid in endoscopic lateral margin assessment. With these techniques, complete resection rates of over 96% have been reported.²⁰ Close follow up with repeat colonoscopy to ensure ablation of any residual neoplasia is recommended at 3 months and again at 1 year following EMR. Residual adenomatous tissue at the time of follow-up is reported between 4 – 14% depending on the expertise of the center.²⁰⁻²² Endoscopic sub-mucosal dissection (ESD) describes a group of techniques and devices that allows en-bloc resection of very large (>20mm) non-polypoid neoplasia. En-bloc resection provides the ability for complete assessment of deep and lateral margins not offered by piece-meal EMR techniques. In centers offering this technique, much lower rates of residual disease are reported (2 versus 14%). The trade-offs however include longer procedure times (108 +/- 71 minutes versus 29 +/- 25 minutes, $p < 0.001$) and an increased risk of perforation (6 vs. 1%), though most perforations can be managed endoscopically.²³ Provided the local expertise and surgical support is available, ESD is the preferred method for complete endoscopic removal of polyps >20mm where there is a high suspicion of early invasive carcinoma, as indicated by a depressed type polyps or surface pit pattern suggestive of superficial invasion. When done by appropriately trained endoscopists, both EMR and ESD, have the benefit of avoiding surgery.

SUMMARY

Flat and serrated polyps can be subtle and challenging to detect, and as a result, likely contributed to the occurrence of interval colorectal cancer after screening colonoscopy.

Detection of non-polypoid colorectal lesions requires recognition of their existence, training in their detection, careful inspection technique and bowel preparation that is adequate to allow their subtle features to be visualized. Referring physicians can assist their patients by providing information on the importance of bowel purgative and by referring them to endoscopists who are known for high quality colonoscopy. Adenoma detection rates are a validated measure of quality in colonoscopy and a predictor of interval colorectal cancer, and therefore can serve as a barometer for this quality.

When a large, flat or otherwise complicated polyp is detected, endoscopic methods offer an alternative to surgery that can reduce the risk and morbidity associated with surgical resection. Referral to a center with both the expertise in endoscopic resection methods (EMR and/or ESD) and adequate surgical support is required to minimize complications. Short interval follow up colonoscopies in the year following endoscopic resection are also needed to ensure complete resection. ■

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