ADVANCES IN ENDOSCOPY

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Serrated Polyps and Synchronous Advanced Neoplasia in Average-Risk Persons

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G&H What is the significance of serrated colon polyps?

XB Serrated colon polyps are a group of heterogeneous lesions characterized histologically by glandular serration (ie, a saw-toothed folding of colonic crypt epithelium). The World Health Organization has classified serrated lesions into 3 general categories (Table).

Historically, serrated polyps were called hyperplastic polyps (HPs) and were thought to have no malignant potential. However, recent data have established that several distinct subtypes of serrated polyps are the precursors of a group of colorectal cancers (CRCs) that exhibit hypermethylation and arise primarily in the proximal colon, the so-called serrated neoplasia pathway, characterized by BRAF mutations and a CpG island methylator phenotype (CIMP). It has been estimated that serrated polyps might be the precursors for approximately 15% to 20% of sporadic CRCs, particularly in the proximal colon, and most CRCs arise through the conventional adenoma pathway characterized by chromosomal instability. Many studies have shown that benign serrated lesions and CIMP-high CRCs share molecular features. In fact, it has been suggested that HPs lead to sessile serrated adenomas/polyps (SSA/Ps) without dysplasia and then dysplasia develops and finally leads to cancer. Moreover, some interval proximal cancers have been attributed to the serrated pathway, emphasizing the need to detect serrated polyps during endoscopic examinations. Therefore, endoscopists should familiarize themselves with detection of these lesions, particularly those that are located in the proximal colon.

G&H How common are the different types of serrated polyps?

XB The most common serrated polyp is the conventional HP, a diminutive, pale, sessile polyp that accounts for 70% to 95% of all serrated polyps and commonly occurs in the rectosigmoid colon, where it is considered to be an innocuous lesion. Sessile serrated lesions are endoscopically similar to the surrounding mucosa of the colon and in the proximal colon are often covered by a mucus cap, rim of debris, or bubbles. The mucus can cause the polyp to appear yellow or rust-colored. SSA/Ps account for 5% to 25% of serrated polyps and occur predominantly in the proximal colon. However, these polyps often appear flat or sessile and are rarely larger than 5 mm. Finally, traditional serrated adenomas (TSAs) are much less common, accounting for only 1% of all colorectal polyps. Although more often described as pedunculated than sessile lesions, they can also be mistaken for flat lesions in the distal colon.

G&H What factors affect detection rates of serrated polyps?

XB Detection rates of serrated polyps vary among endoscopists, indicating that these lesions are significantly underdiagnosed and that their detection is highly operator-dependent. Differences in detection rates can be explained by several factors: cecal intubation, withdrawal time, quality of bowel cleansing, preparation, field of view (eg, 140° vs 170°), colonoscope definition, use of a plastic cap, timing of the colonoscopy (morning vs afternoon), or use of antispasmodic agents. A recent study showed that at least 1

Table. Pathologic Classification of Serrated Polyps

Hyperplastic Polyps
• Goblet cell hyperplastic polyps
• Microvesicular hyperplastic polyps
• Mucin-poor hyperplastic polyps
Sessile Serrated Adenomas/Polyps*
• With or without cytologic dysplasia
Traditional Serrated Adenomas

*Sessile serrated adenomas and sessile serrated polyps are considered to be synonymous.

proximal serrated polyp was detected in 1% to 18% (average, 13%) of colonoscopies, for a colonoscopy detection rate of 0.01 to 0.26. In addition, a strong correlation was observed between adenoma detection rates and proximal serrated polyps. Although there is no current standard proximal serrated polyp detection rate, based on these study findings, a serrated detection rate of 5% has been suggested when the adenoma detection rate is around 20%. A recent prospective study found that withdrawal time was strongly and significantly associated with proximal serrated polyp detection (average, 12%; range, 6% to 22%). Several studies have suggested that large and dysplastic serrated polyps in the proximal colon were nonpolypoid more often than distal serrated polyps, making the former group more likely to be overlooked. Another important issue is the recent finding that up to 31% of all SSA/Ps are incompletely resected.

G&H Is there an association between serrated polyps identified during colonoscopy and synchronous advanced neoplasia in average-risk persons?

XB Several recent studies have evaluated the significance of large (≥10 mm) proximal serrated polyps in patients who do not meet the criteria for serrated polyposis syndrome and the relationship of these polyps to the development of CRC. These studies have shown that large serrated polyps (LSPs) and the proximal serrated location were independent predictors of synchronous advanced neoplasia and CRC (2 to 5 times greater odds). Of greater clinical impact, one study showed that there was a relationship between the detection of proximal nondysplastic serrated polyps and an increased risk for interval neoplasia during surveillance. In addition, my colleagues and I conducted a large, nationwide, population-based, multicenter, randomized, controlled trial of average-risk persons (the Colonprev study), which showed that LSPs, but not proximal serrated lesions, were an independent risk factor for the development of synchronous advanced colorectal neoplasia. Furthermore, the risk of LSPs was similar to that of the presence of at least 3 small tubular adenomas and higher than the risk associated with any small tubular adenomas. These findings were similar to those of a recently published study from The Netherlands, which found a relationship between proximal and large HPs and synchronous advanced colorectal neoplasia. As far as I know, these 2 studies were the first to observe a relationship between proximal HPs and synchronous advanced neoplasia. Further studies are warranted to determine whether large proximal HPs also have a relationship with synchronous advanced colorectal neoplasia.

G&H What is the take-home message from these studies for community colonoscopists?

XB The take-home message is, first, that in average-risk persons, the presence of large serrated polyps (≥10 mm) is an independent risk factor for the development of synchronous and metachronous advanced colorectal neoplasia. Second, although further studies are needed, the presence of proximal HPs is also related to the presence of synchronous advanced colorectal neoplasia. The recent recommendation by an expert panel to remove all proximal serrated polyps appears to be endorsed by these study findings. Because it is thought that low proximal serrated polyp detection rates are associated with a higher risk of interval cancer, additional training to detect and completely remove these lesions could be beneficial.

G&H Should adjunctive techniques be used to help identify serrated polyps?

XB Significant progress has been made in colonoscopy imaging with the development of new strategies, such as pancolonic chromoendoscopy (Figure), narrow-band imaging (NBI), ultramagnification systems, and confocal laser endomicroscopy. The improved ability to differentiate lesions during endoscopy allows for real-time polyp removal. For example, the ability to recognize SSA/Ps may allow endoscopists to select the resection technique that ensures complete removal of the lesions. In addition, being able to identify the histologic type of small HP lesions in the rectosigmoid area may allow endoscopists to discard or leave these lesions in situ, which would reduce costs and workloads without being accompanied by an increased risk of potential in situ neoplastic lesions. High-resolution endoscopy, chromoendoscopy, and NBI can help visualize polyp pit patterns, which aids in the differentiation of HPs from other types of polyps. (A novel pit pattern, referred to as type II-open, has been described as having high specificity [97%] and moderate sensitivity [65%] for identifying SSA/P.) New technologies such as probe-based confocal laser endomicroscopy are emerging for in vivo imaging, which may enable endoscopists to interpret the mucosal surface.

Although some studies have shown a statistically significant increase in the overall detection rate for polypoid and flat adenomas as well as serrated lesions when comparing

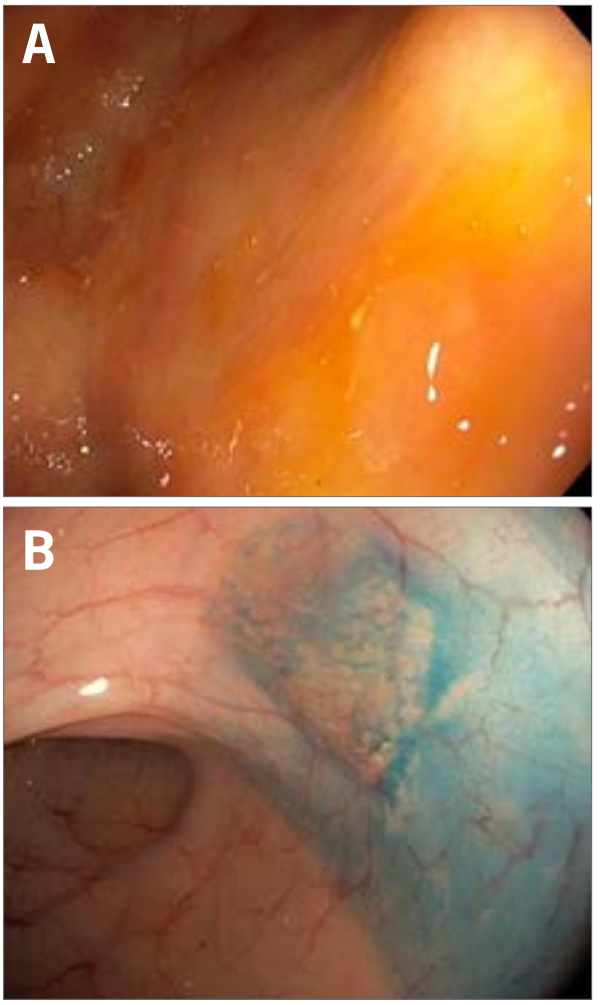

Figure. A flat sessile serrated adenoma/polyp in the proximal colon under white light **(A)** and chromoendoscopy **(B)**, the latter of which shows better demarcation.

chromoendoscopy with standard colonoscopy, a retrospective study by Kahi and colleagues did not observe differences in proximal serrated polyp detection when comparing high-definition chromocolonoscopy and high-definition white-light colonoscopy (17.6% vs 21.9%; *P*=.34). Another recent prospective study did not identify factors that commonly influence colonoscopy performance (field of view, colonoscope definition, or use of a plastic cap) as being significantly associated with proximal serrated polyp detection. Therefore, to optimize colonoscopic detection of serrated polyps, it is essential to use high-quality bowel preparation and adequate luminal distension with careful and complete mucosal inspection as well as diligent washing to remove debris and slow colonoscopic withdrawal.

G&H What are the current screening guidelines for serrated polyps?

XB The main goal of CRC screening and surveillance is to prevent and reduce cancer mortality by detecting and removing precancerous lesions and cancers at an early stage. Until recently, there were no specific guidelines for the management of serrated polyps. In 2012, 2 groups emphasized the importance of these polyps and incorporated them into postpolypectomy surveillance recommendations. The US Multi-Society Task Force on Colorectal Cancer released updated guidelines on the management of serrated polyps, and an expert consensus panel published recommendations based on advancements and insights from recent published literature. However, both guidelines were based on expert consensus opinion rather than good-quality evidence, and no longitudinal data have been available to define postpolypectomy surveillance until now. Both guidelines defined high-risk groups for development of advanced neoplasia during surveillance as those with a TSA, a SSA/P with cytologic dysplasia, or a large (≥10 mm) SSA/P. However, the expert panel proposed surveillance intervals depending not only on polyp histology but also on size, number, and location. Surveillance intervals for HPs located proximal to the sigmoid colon or those based on the size and number of HPs or SSA/Ps are only reported in the consensus expert guidelines.

G&H What are the next steps in research?

XB Currently, several studies are underway to assess the role of endoscopic techniques such as NBI for improving the detection of serrated polyps (specifically proximal serrated polyps). Larger longitudinal and molecular-based studies are needed to clarify the so-called serrated neoplasia pathway and its molecular biology. Finally, high-quality prospective trials are required to elucidate the rate of progression of serrated polyps and to inform the improvement of surveillance strategies for patients with these lesions.

Dr Bessa has no relevant conflicts of interest to disclose.

Suggested Reading

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