EDITORIAL

Prediction of colorectal polyp pathologic lesions with image-enhanced endoscopy: What will it take to make it matter?

In this issue of *Gastrointestinal Endoscopy,* Wallace et al[1] report a randomized comparison of the Olympus 180 and 190 colonoscopes for predicting the pathologic character of colorectal polyps. The 190 is the new version of the Olympus colonoscope, and its new features include pushbutton-operated optical magnification, which increases magnification from the ×30 provided by the 180 system to about ×65. By comparison, some magnification colonoscopes, including instruments made by Olympus, provide ×100 to ×125 magnification. Therefore, the level of magnification provided by the 190 colonoscope is intermediate between the 180 colonoscope and the highest-magnification colonoscopes available. The 190 magnified image provided no advantage over 180 imaging for accuracy of prediction of polyp pathologic lesions. In addition, there was no benefit from the use of narrow-band imaging (NBI) compared with white light. Accuracy was higher when polyps were interpreted with high confidence.

Wallace et al[1] also tested whether the 180 and 190 colonoscopes provided accuracy that met the American Society for Gastrointestinal Endoscopy (ASGE) Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) criteria for real-time interpretation of diminutive colorectal polyp pathologic lesions. Three years ago, the ASGE proposed 2 clinical uses for real-time endoscopic prediction of pathologic polyp lesions (Table 1) and set thresholds for accuracy that technologies should achieve to be used as alternative treatment paradigms to the current management of these clinical problems based on pathologic assessment.[2] The endpoint at which polyps have their pathologic character predicted by endoscopic criteria and are then discarded without submission to pathologic assessment is commonly called "resect and discard" (Table 1). Wallace et al[1] found that the 180 and 190 imaging colonoscopes each allowed accuracy that exceeded the PIVI thresholds for both clinical endpoints described in Table 1.

COMPARISON OF THE CURRENT RESULTS WITH THOSE OF PREVIOUS STUDIES

Two previous studies, 1 randomized[3] and 1 not,[4] have compared the 180 and 190 colonoscopes for prediction of polyp pathologic lesions. Both studies found that the 190 system had comparable accuracy to the 180 system,[3,4] (ie, the same conclusion reached by Wallace et al). Unlike Wallace et al, both prior studies found that the 190 resulted in more polyps being interpreted with high confidence, which could result in relative cost savings compared with the 180 colonoscope in a "resect and discard" policy. The nonrandomized study found that NBI had superior accuracy to white light for both the 180 and 190 systems,[4] which was not addressed in the other randomized trial[3] and was unlike the result of Wallace et al. Most previous studies have found that NBI permits better accuracy than white light.[5] Like Wallace et al, both prior studies found that both the 180 and 190 colonoscopes allowed both PIVI thresholds to be reached.[3,4]

Wallace et al found that the 180 and 190 imaging colonoscopes each allowed accuracy that exceeded the PIVI thresholds.

There is now a large literature reporting the accuracy of various technologies for prediction of a polyp as a pathologic lesion. In a meta-analysis, Wanders et al[6] identified 91 studies addressing the issue, including 56 of NBI, 10 of the Pentax i-SCAN, 14 of the Fujinon Intelligent Chromoendoscopy system (FICE), 11 of autofluorescence, and 11 of confocal laser microscopy. They concluded that all of the technologies were adequate for routine practice, although confocal laser microscopy had slightly higher sensitivity, and autofluorescence had lower specificity. In another meta-analysis, McGill et al[7] concluded that NBI provides accuracy that meets both the ASGE PIVI thresholds. Recently, advocates of resect and discard have been disappointed to see studies from community-based endoscopists in which the ASGE PIVI thresholds were not met.[8,9] However, the study by Wallace et al adds to those from academic practice showing that NBI allows high accuracy in polyp differentiation and for the PIVI thresholds to be met.[10,11]

WHAT TYPES OF INFORMATION CAN ENDOSCOPIC IMAGING AND PATHOLOGISTS PROVIDE ABOUT COLORECTAL POLYPS?

The overwhelming majority of colorectal polyps fall into 2 histologic categories: the conventional adenomas and

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TABLE 1. The American Society for Gastrointestinal Endoscopy Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) paradigms for alternative management strategy for diminutive polyps detected at colonoscopy

Paradigm 1. Resect and discard. A technology should allow ≥90% agreement between intervals selected for postpolypectomy surveillance based on (1) high-confidence endoscopic prediction of pathologic lesions for those ≤5 mm followed by resection and no submission to pathologic assessment combined with pathologic assessment for all lesions >5 mm and those <5 mm interpreted endoscopically with low confidence and (2) intervals selected based on pathologic assessment of all polyps. When this agreement threshold is met, the technology is an appropriate tool for a resect-and-discard paradigm as an alternative to submission of all diminutive polyps for pathologic assessment.
Paradigm 2. Leave distal colon hyperplastic polyps in place. A technology should allow a negative predictive value ≥90%, when predictions are made with high confidence, for adenomas ≤5 mm in the rectosigmoid colon. When this threshold is met, then the technology can be used to leave distal colon polyps in place without resection or biopsy.

Adapted from Rex DK, Kahi C, O'Brien M, et al. The American Society for Gastrointestinal Endoscopy PIVI (Preservation and Incorporation of Valuable Endoscopic Innovations) on real-time endoscopic assessment of the histology of diminutive colorectal polyps. Gastrointest Endosc 2011;73:419-22.

the serrated class.[12] Conventional adenomas are uniformly dysplastic (classified as low or high grade) and are also characterized as tubular, tubulovillous, or villous. The serrated class includes the hyperplastic polyps, sessile serrated polyps (SSPs, also known as sessile serrated adenomas), and traditional serrated adenomas (TSAs). Endoscopic imaging is effective at separating lesions into the conventional adenoma versus the serrated class, but it is not capable at this time of subtyping conventional adenomas by dysplasia grade or villosity and similarly is not reliably capable of subdividing serrated lesions into hyperplastic polyps versus SSPs. This is particularly true of the pushbutton-operated, easy-to-use technologies that are standard equipment on commercial colonoscopes (NBI, FICE, and i-SCAN) and that rely on interpretation of surface structures including microvessels.[13,14] An exception to this generality is the presence of large open pits on serrated lesions (type O pits), which is specific to but not sensitive for SSP.[15] Of course, there are other features such as proximal location, large size, and mucus cap that favor SSP over hyperplastic polyp,[16,17] but these are different considerations from the endoscopic prediction of a pathologic lesion from microscopic surface features. Endoscopic imaging is also good at identifying deep submucosal invasion by cancer in polyps.[18] In many cases, cancer can be predicted from gross morphologic features such as ulceration, but deep submucosal invasion is also typically accompanied by disruption of the surface vascular pattern, so that the surface vessels and structures have an irregular or amorphous pattern. Thus, endoscopic imaging has both strengths and limitations.

What is often not appreciated is that endoscopists and pathologists have similar limitations. Pathologists are quite reliable for separating conventional adenomas from the serrated class and for identifying cancer in polyps.[19] By contrast, the level of interobserver variation among pathologists in interpreting dysplasia grade and villous elements is so great that the British Society of Gastroenterology does not consider these factors in its postpolypectomy surveillance recommendations.[20] The problem is accentuated to a remarkable degree in small adenomas, where high-grade dysplasia and villous elements are uncommon.[21] Similarly, differentiation of SSP from hyperplastic polyp is unreliable even among expert pathologists,[22] and in clinical practice there are pathologists who *never* read SSPs.[23] TSA, the only uniformly dysplastic lesion in the serrated class, is so consistently misread in clinical practice as tubulovillous adenoma that anecdotally I encounter many endoscopists who have never seen TSA on a pathology report.

The approach to these issues by the ASGE was to limit the target polyps for resect and discard and for leaving distal hyperplastic polyps in place to those 5 mm or smaller.[2] Polyps in that size range have a cancer risk near zero and have a low prevalence of the histologic features that both endoscopists and pathologists have difficulty recognizing: villous elements, high-grade dysplasia, and SSP components.

WHAT ARE THE POTENTIAL BENEFITS OF THE PIVI POLYP PARADIGMS?

The main gains from the PIVI paradigms for diminutive polyp management are cost savings. The potential savings from resect and discard were estimated at more than $1 billion per year in the United States.[24] As high-definition colonoscopes[25] and split-dose bowel preparation[26] become commonplace the savings would increase. Leaving distal diminutive hyperplastic polyps in place saves the costs of both pathologic assessment and polypectomy, and it reduces patient risk, at least when endoscopists use electrocautery to resect diminutive polyps. Some have argued that resect and discard would allow colonoscopists to tell patients immediately when the next colonoscopy would occur, which might improve adherence to the follow-up examination, but this is speculative at this time.

WHAT ARE THE RISKS OF THE PIVI POLYP PARADIGMS?

One risk is that a cancer in polyp 5 mm or smaller would be discarded and not recognized. If this cancer had deep submucosal invasion it might recur in the colon wall or a