

## Colonoscopy: As Good as Gold?

But al thing which that shineth as the gold

Nis nat gold, as that I have herd it told

—Geoffrey Chaucer, *Canterbury Tales* (1387)

All that glitters is not gold;

Often have you heard that told

—William Shakespeare, *Merchant of Venice* (1596–1597)

As good as gold . . .

—Charles Dickens, *A Christmas Carol* (1843)

Although William Shakespeare's reputation may be slightly tarnished by the knowledge that he probably borrowed from Chaucer, he is, nevertheless, the bard against whom we compare all others. In gastroenterology, it has been a foregone conclusion that colonoscopy can provide the most accurate examination of the colon, and it is the gold standard against which we judge other tests. With the increasing use of colonoscopy in colon cancer screening as a primary test or a test after a positive screening result with fecal occult blood test, sigmoidoscopy, computed tomography colonography, or fecal DNA testing, knowing the true accuracy of colonoscopy takes on even greater importance.

In previous studies of colonoscopy accuracy (1, 2), patients had 2 colonoscopy examinations performed by different endoscopists (gold vs. gold). Colonoscopy seldom missed polyps greater than 1 cm (miss rate, 0% to 6%). These studies are biased toward agreement between the first and second colonoscopy—and therefore toward overestimating sensitivity and specificity—because factors leading to a miss on the first examination (such as a polyp hiding behind a fold) are likely to be similar during the second examination. Pickhardt and colleagues (3, 4) cleverly evaluated the sensitivity and specificity of optical colonoscopy (OC) by performing virtual colonoscopy (VC) followed by OC. After the endoscopist examined each segment of the colon, the results of VC were revealed. If a polyp was present on VC but not on OC, the endoscopist reexamined the segment. If the endoscopist found a polyp on the second examination, the polyp was classified as a missed lesion by OC (false-negative). Endoscopists missed 10% of neoplastic polyps that measured 6 mm or greater ( $n = 21$ ), including 6 of 51 (11.8%) adenomas measuring greater than 9 mm and 1 cancerous polyp. In this issue, Pickhardt and colleagues (4) add crucial information about the causes of missed polyps: 20 of 21 missed adenomas in their study were located on a fold or in the rectum. The location of the polyp on the fold may be important. Most missed polyps were on the proximal side of a fold that would be hidden from endoscopic view.

This study probably overestimates the sensitivity of OC as practiced in the community or as done by an undertrained endoscopist. One might imagine that the endoscopists in the study were especially careful during the first examination, knowing that their performance would be assessed. Another recent study compared VC and OC (5) by using a similar method of segmental unblinding as the gold standard. Optical colonoscopy fared better in this study. Endoscopists detected 96% of polyps greater than 9 mm. The reasons for the discrepancy between this study and the study by Pickhardt and colleagues are not apparent.

The miss rate for OC is not surprising. Several previous studies reported clinically significant colonic neoplasia within 3 years of a “clearing” colonoscopy, during which the endoscopist removed all visible polyps (6–8). In the follow-up colonoscopic examinations, 6% to 11% colonoscopies revealed advanced adenomas (defined as polyps > 1 cm or with villous change) and 0.7% to 0.9% revealed cancer. The baseline examination probably missed some of these important lesions. In addition to missing lesions behind folds, the baseline examination may have missed flat, depressed lesions on both VC and OC. Even under ideal conditions, colonoscopy is not perfect.

How can we improve the quality of colonoscopy? A task force of professional organizations in gastroenterology recommended quality indicators for colonoscopy (9). Endoscopists should be able to intubate the cecum in 90% to 95% of procedures; this requires a skill that is directly related to the intensity of training. A recent study of colonoscopy in the United Kingdom (10) found that endoscopists could document a complete colon examination to the cecum in only 57% of colonoscopies. The authors attribute this finding to poor training in the United Kingdom, where the average endoscopist performs fewer than 100 supervised procedures during training. In the United States, studies demonstrate that 200 is the minimum number of supervised procedures that should be performed during training (11–13). Physicians who perform colonoscopy should meet this standard. Second, the critical part of a colonoscopic examination is withdrawal of the instrument. Rapid withdrawal time (<6 to 10 minutes) results in a higher rate of missed lesions (14). The current report about the location of missed polyps reinforces this point (4). A meticulous examination behind folds and in the rectum should be routine. Future advances in colonoscopy, including magnification and chromoendoscopy (with vital stains) or improved bowel preparations, may further enhance the quality of colonoscopy.

Are there enough fully trained endoscopists to meet the demand for colonoscopy if the public accepts colorectal cancer screening? Currently, only 30% to 40% of individuals older than 50 years of age receive recommended colon

screening. According to some analyses, increased adherence to screening recommendations would exceed available endoscopic resources (15).

Could VC be used as a primary screening test to target patients who are most likely to benefit from OC, thereby reducing the colonoscopy workload? Virtual colonoscopy is still an evolving technology, and many questions remain. First, can other investigators reproduce the promising results reported by Pickhardt and colleagues (4) in diverse clinical settings (generalizability)? Second, what is the minimum size of lesions revealed on VC that should trigger referral of patients for OC? If all patients with polyps of any size are referred for OC, VC will not be cost-effective (16). Pickhardt and colleagues found that VC revealed at least 1 polyp in 622 of 1233 patients (50.4%) (3). Although small polyps are seldom malignant when first identified, the natural history of small polyps is largely unknown, since most are removed when detected. In a commentary, Pickhardt suggested using VC to follow small polyps noninvasively (17). Although this suggestion may be rational, many patients will object when their physician tells them that VC showed a polyp and then propose to monitor its growth with another VC in the future. After years of telling patients that polyps are cancer precursors, the medical community will need to reeducate the public to accept leaving polyps in place. Many patients and physicians may be uncomfortable with this approach until careful studies show that monitoring polyp growth with VC is a safe strategy. We also need to determine the appropriate interval for performing VC to monitor polyp growth.

Third, although the radiation exposure in VC is considered to be low (5 to 10 mSv), repeated examinations will lead to substantial cumulative radiation exposure (18). Higher radiation exposure is associated with excess cancer mortality. A recent analysis of computed tomography screening for lung cancer calculated an excess mortality from radiation-related lung cancer (19). Such analyses are needed for VC, particularly if we envision using repeated studies to monitor polyp growth.

Fourth, virtual colonoscopy commonly identifies extracolonic findings (20). Although VC has identified cases of early renal-cell or ovarian cancer as an incidental finding, few findings in asymptomatic patients will be clinically important (20). We don't know the cost, morbidity, and mortality of evaluating these findings in otherwise asymptomatic patients. Until we resolve these issues, I do not think VC is ready for widespread use as a screening test or as a test to monitor polyp growth.

Colonoscopy, as a gold standard, has lost some of its glitter. Nevertheless, it remains the preeminent test for diagnosing and treating colonic neoplasia. As an endoscopist, I find the data on colonoscopy accuracy to be a humbling reminder of the limitations of colonoscopy and an urgent call to improve quality by demanding excellent training and adherence to published quality indicators.

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