Flat Colorectal Lesions in Asymptomatic Adults: Implications for Screening with CT Virtual Colonoscopy

OBJECTIVE. The clinical significance of flat lesions in colorectal cancer screening remains uncertain. The purpose of this study was to investigate the frequency, histology, and virtual colonoscopy detection of flat lesions in an asymptomatic screening population.

SUBJECTS AND METHODS. The morphology of all detected polyps was prospectively recorded as flat or polypoid (sessile or pedunculated) in 1,233 consecutive asymptomatic adults who underwent same-day virtual colonoscopy and optical colonoscopy. A flat morphology was defined as a shallow plaquelike broad-based lesion with a height of less than one half of its width.

RESULTS. Of 344 polyps of 6 mm or greater confirmed at optical colonoscopy, 17 (4.9%) were labeled as flat at both virtual colonoscopy and optical colonoscopy; 17 (4.9%), at optical colonoscopy only; and 25 (7.3%), at virtual colonoscopy only, yielding 59 total lesions in 52 (4.2%) of 1,233 patients. Twenty-nine (49.2%) of 59 flat lesions were adenomatous, of which four measured 10 mm or greater and one 6- to 9-mm lesion was histologically advanced. None of the 148 diminutive flat lesions (≤5 mm) detected at optical colonoscopy was histo- logically advanced. Virtual colonoscopy prospectively detected 24 (82.8%) of 29 flat adenomas and 47 (80.0%) of all 59 flat lesions 6 mm or greater. In comparison, the sensitivity of virtual colonoscopy for the detection of polypoid adenomas and all polypoid lesions of 6 mm or greater was 86.2% (156/181, \(p = 0.58\)) and 81.0% (231/285, \(p = 0.86\)), respectively.

CONCLUSION. Flat adenomas measuring 6 mm or greater are uncommon in a typical Western screening population, and advanced flat neoplasms are rare. The sensitivity of virtual colonoscopy for detecting flat lesions was similar to that of polypoid lesions. These results indicate that flat lesions are not a significant drawback for virtual colonoscopy screening.

There has been considerable debate among gastroenterologists regarding the prevalence and significance of small but aggressive flat colorectal adenomas [1–6]. Because these lesions may be more easily missed at optical colonoscopy, investigators in Japan developed advanced techniques for optical colonoscopy detection (e.g., chromoscopy with magnification) [7]. Other investigators, however, have argued that small flat adenomas with increased malignant potential are rare in Western countries and do not warrant widespread implementation of such special techniques [4–6].

Similar to their appearance at optical colonoscopy, flat lesions are also less conspicuous at CT virtual colonoscopy compared with polypoid lesions and could be a weakness for primary virtual colonoscopy screening. Although virtual colonoscopy detection of flat lesions has been studied in smaller high-risk populations [8, 9], it has not, to our knowledge, been investigated in an asymptomatic screening population. The primary goals of this study were to report the frequency and histology of flat colorectal lesions in an asymptomatic Western screening population and also to assess the ability of virtual colonoscopy to detect flat lesions in this setting.

Subjects and Methods

Patients

Our study protocol for same-day virtual colonoscopy and optical colonoscopy was approved by the institutional review board at all three participating medical centers. All subjects provided written informed consent to participate in the trial. The study group comprised asymptomatic adults 50–79 years old (40–79 years if family history positive for colorectal cancer was reported)
referred for colorectal cancer screening. Exclusion criteria included a stool guaiac test positive for blood or iron deficiency anemia within the past 6 months; rectal bleeding, hematochezia, or unintentional weight loss of more than 10 lb (4.5 kg) within the past 12 months; optical colonoscopy within the past 10 years or barium enema within the past 5 years; history of adenomatous polyps, colorectal cancer, or inflammatory bowel disease; and family history of familial adenomatous polyposis or nonpolyposis cancer syndromes.

A total of 1,233 consecutive asymptomatic adults (505 women, 728 men; mean age, 57.8 years) successfully completed same-day virtual colonoscopy and optical colonoscopy over a 14-month period. The overall virtual colonoscopy performance data for this cohort have been published previously [10], but an analysis of polyps according to morphology was beyond the scope of that clinical report and has not, to our knowledge, been previously reported.

Virtual Colonoscopy
Study participants underwent colonic cleansing with oral intake of 90 mL of sodium phosphate (Phospho-Soda, Fleet) the day before virtual colonoscopy and optical colonoscopy examinations. Patients also consumed 500 mL of dilute barium (2.1% by weight) and 120 mL of water-soluble iodinated contrast material for the purposes of stool tagging and electronic fluid subtraction [11]. Our CT protocol and virtual colonoscopy interpretation technique have also been detailed previously [10]. In summary, colonic distension was achieved with patient-controlled insufflation of room air. Breath-hold supine and prone CT acquisitions were obtained on 4- and 8-MDCT scanners (LightSpeed Plus and LightSpeed Ultra, GE Healthcare). The CT technique entailed 1.25- to 2.5-mm collimation, 13.5- to 15-mm/sec table speed, 1-mm reconstruction interval, 100 mA, and 120 kVp.

Virtual colonoscopy studies were prospectively interpreted using a commercially available CT colonography system (V3D Colon, version 1.2, Viatronix). This system isolates the colon and rectum, electronically subtracts any residual opacified fluid, and generates an automated centerline as routine postprocessing steps. The 3D endoluminal fly-through images were used for primary polyp detection, and the 2D images were used mainly for confirmation and problem solving. Each virtual colonoscopy study was reviewed prospectively by one of six radiologists from one of the three participating medical centers trained in the primary 3D approach. The average virtual colonoscopy interpretation time (including evaluation of extracolonic structures) was less than 20 min [10].

Polyp morphology was prospectively assessed as being flat or polypoid (including both sessile and pedunculated polyps). Analogous to its appearance at optical colonoscopy, a flat polyp was defined as a shallow plaquelike broad-based lesion with a height of less than one half of its width. Except for some larger lesions, these flat lesions generally measure 3 mm or less in height. Any polyp deemed to have a flat morphology on virtual colonoscopy or optical colonoscopy or both was considered to be a flat lesion for our analysis, with the exception of virtual colonoscopy–detected flat lesions that were unmatched at optical colonoscopy because histologic evaluation was not possible for these potential lesions. Polyps were measured on 3D images using electronic calipers, and measurements were recorded by segment. Given their lack of clinical significance, polyps measuring less than 5 mm were generally ignored on virtual colonoscopy [10, 12].

Optical Colonoscopy
Optical colonoscopy was performed by experienced colonoscopists using standard commercial video colonoscopes on the same day as virtual colonoscopy, immediately after prospective virtual colonoscopy interpretation. Advanced techniques to elucidate flat colorectal lesions, such as dye spraying or magnification, were not used. However, even if some flat lesions are being missed by the standard virtual colonoscopy technique in screening populations in Western countries, there is little evidence that significant lesions (i.e., advanced adenomas or cancers) are undetected [4–6]. The colonoscope was advanced to the cecum and then sequentially withdrawn into more distal segments for polyp detection. Polyps were measured using a calibrated linear probe, which has been shown to be more accurate than either visual or biopsy forceps estimation [13]. Unlike in the procedure for virtual colonoscopy, we measured, recorded, and retrieved polyps less than 5 mm at optical colonoscopy. Of note, the dilute barium used in the preparation did not adversely affect the optical colonoscopy examination.

As with its assessment on virtual colonoscopy, polyp morphology was prospectively assessed as being flat, sessile, or pedunculated. After the colonoscopist completed evaluation of a given segment, a study nurse unblinded the virtual colonoscopy results. If a polyp that measured 5 mm or greater was detected on virtual colonoscopy but not on initial optical colonoscopy, the colonoscopist closely reexamined that segment and was allowed to review the virtual colonoscopy images for guidance. This technique of “segmental unblinding” results in an enhanced reference standard compared with prospective optical colonoscopy alone.

Histologic Analysis
All polyps retrieved from optical colonoscopy were sent for histologic analysis, and each was evaluated by an experienced pathologist. Polyps were broadly divided into adenomatous and nonadenomatous histologies. An advanced neoplasm was defined as any adenoma measuring 10 mm or greater in diameter or showing high-grade dysplasia, a prominent villous component, or a focus of cancer [14].

Results
Of 344 polyps retrieved at optical colonoscopy that measured 6 mm or more in diameter, 17 (4.9%) were designated as flat at both virtual colonoscopy and optical colonoscopy, 17 (4.9%) were deemed flat at optical colonoscopy only, and 25 (7.3%) were flat at virtual colonoscopy only. All matched lesions labeled as flat by only one study were labeled as sessile on the other (i.e., not pedunculated). Virtual colonoscopy prospectively detected 47 (80.0%) of the 59 flat lesions. In comparison, the sensitivity of virtual colonoscopy for all polypoid (nonflat) lesions 6 mm or greater was 81.0% (231/285, p = 0.86). Five flat lesions (8.5%) were missed at the prospective optical colonoscopy evaluation but found after unblinding of the virtual colonoscopy results.

At histopathologic examination, 29 (49.2%) of the 59 flat lesions 6 mm or greater were adenomatous (Fig. 1) and accounted for 13.8% (29/210) of all adenomas 6 mm or greater. Five of these neoplasms were advanced on the basis of size (n = 3), histology (n = 1), or both (n = 1). One large cecal mass with a flat morphology was frankly malignant (Fig. 2). The single advanced lesion of less than 1 cm showed a prominent villous component. None of the flat adenomas had a central depression (depressed adenoma) but were instead the flat elevated form. Virtual colonoscopy prospectively detected 24 (82.8%) of 29 flat adenomas, compared with 156 (86.2%) of 181 polypoid (nonflat) adenomas; the difference was not statistically significant (p = 0.58). Using a by-patient analysis and a polyp size threshold of 6 mm, we found that only four patients (0.3%)
with a flat adenoma had false-negative results on virtual colonoscopy. Missed lesions could be identified in two of these cases on retrospective review. None of the adenomas in these patients was an advanced lesion.

Of the 30 nonadenomatous flat lesions of 6 mm or greater, 26 (86.7%) were hyperplastic at pathologic examination (Fig. 3); the remaining lesions were normal colonic mucosa. Virtual colonoscopy prospectively detected 23 (76.7%) of these 30 nonadenomatous lesions. Eight nonadenomatous flat lesions measured 10 mm or greater at virtual colonoscopy or optical colonoscopy or both, including six hyperplastic polyps and two areas of normal colonic mucosa. Virtual colonoscopy prospectively missed three nonadenomatous lesions measuring 10 mm or more at optical colonoscopy (Fig. 3), including two hyperplastic lesions and one 80-mm lesion that revealed only normal colonic mucosa at histologic evaluation.

Of 1,233 virtual colonoscopy examinations, a flat lesion measuring 10 mm or greater was prospectively identified in only 11 instances (0.9%). In five of these 11 cases, a matching lesion was found at optical colonoscopy, yielding a positive predictive value of 45.4%, compared with 69.2% (72/104) for polypoid morphologies.

Fig. 1.—58-year-old asymptomatic man with 6-mm flat sigmoid adenoma detected at both virtual and optical colonoscopy. A, Three-dimensional endoluminal image from virtual colonoscopy shows slightly elevated lesion (arrowheads). B, Two-dimensional axial image obtained using soft-tissue window settings confirms small flat soft-tissue lesion (arrowhead). C, Digital photograph from optical colonoscopy shows same flat lesion (arrowheads), which was tubular adenoma at pathologic evaluation. Note adjacent calibrated linear probe used for polyp measurement.

Fig. 2.—72-year-old asymptomatic man with flat cecal adenocarcinoma. A, Three-dimensional endoluminal image from virtual colonoscopy shows slightly lobulated but predominately flat mass (arrowheads) that appears to focally thicken a colonic fold. This lesion measured more than 4 cm at both virtual and optical colonoscopy. B, Two-dimensional axial image also shows flat cecal soft-tissue mass (arrowhead). C, Digital photograph from optical colonoscopy shows same large flat lesion (arrowheads) as seen in A and B.
At optical colonoscopy, 148 (15.3%) of 966 diminutive lesions (≤ 5 mm) were recorded as flat. At pathologic examination, 41 (27.7%) of these were adenomatous and 107 (72.3%) were nonadenomatous. None of the diminutive flat adenomas was histologically advanced. Of 26 lesions measuring 6–9 mm that were labeled flat at optical colonoscopy, none was histologically advanced and 15 (57.7%) were nonadenomatous.

Discussion

The true frequency and significance of small but histologically aggressive flat adenomas have been a source of much debate since the report by Muto et al. in 1985 [1]. Some investigators, predominately in Japan, have suggested that these lesions are relatively common and may be an important de novo pathway to malignancy that is separate from the standard polyp–carcinoma progression [2, 3]. These lesions, which may appear slightly raised or completely flat or may contain a central depression, are more difficult to detect at optical colonoscopy. This problem has given rise to advanced techniques such as mucosal dye spraying with indigo carmine (chromoscopy) and magnification colonoscopy [7].

The reported frequencies of flat adenomas have varied widely, but most studies, including ours, have found that they account for approxi-
Although sensitivity for detection is of primary importance with regard to virtual colonoscopy performance with flat lesions, specificity is often overlooked but is also important. Adherent stool, which is the major source of false-positive findings on virtual colonoscopy, often manifests as a flat lesion. It is for this reason that we believe that contrast tagging with barium is vital because it allows one to easily distinguish adherent stool from a true flat lesion [11] (Fig. 4). Translucency rendering, which allows rapid assessment of the internal density of a lesion on the 3D display, can efficiently exclude tagged stool without the need for a time-consuming 2D correlation (Fig. 4C) [22].

A major limitation of our study was the difficulty in enforcing consistent application of the definition for a flat lesion among virtual and optical colonoscopists, particularly among colonoscopists, who had a tendency to use a gestalt approach in identifying what represents a flat colorectal lesion. This difficulty may help explain why so many matching lesions labeled as flat on virtual colonoscopy were recorded as sessile by the colonoscopist. Regardless, the sensitivity of virtual colonoscopy for flat lesions would not likely have changed much because there is little difference between flat and polypoid detection rates.

In summary, our findings suggest that in an asymptomatic Western screening population, small flat adenomas are uncommon and rarely harbor aggressive histologic features. This finding is further evidence that small polyps detected at virtual colonoscopy can be safely followed up with virtual colonoscopy surveillance without the need for polypectomy until significant growth, which will occur in only a minority of cases, is encountered [23, 24]. Furthermore, virtual colonoscopy is a sensitive technique for detecting nondminimative flat lesions, particularly flat adenomas. These results indicate that flat colorectal lesions are not a significant drawback for primary virtual colonoscopy screening.

References
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