MAYO CLINIC

EDITORIAL

June 2007
Volume 82
Number 6

Mayo Clinic Proceedings

Colonic Preparation for Computed Tomographic Colonography: Understanding the Relative Advantages and Disadvantages of a Noncathartic Approach

Colorectal cancer (CRC) remains the second-leading cause of cancer-related deaths in the United States despite the fact that it is believed to be largely preventable through effective screening. The main reason for this troubling paradox is the continued poor compliance associated with current approaches to screening. Computed tomographic (CT) colonography is an emerging diagnostic test that has the potential to provide another effective CRC screening option. However, to achieve any real benefit, a new test must succeed in attracting additional patients to undergo screening. Although CT colonography screening offers a number of relative advantages over optical colonoscopy (eg, less invasive, less costly, safer, yet equally sensitive for relevant pathology), potential drawbacks include the lack of therapeutic ability and the continued need for cathartic preparation. In this issue of *Mayo Clinic Proceedings*, Beebe et al[1] report that one third of survey respondents identified the laxative preparation as the "most troublesome part of CRC screening." Therefore, at first glance, one might reasonably assume that a laxative-free approach to CT colonography represents something of a "holy grail" for CRC screening. However, although validation of noncathartic CT colonography for screening would undoubtedly represent a welcome addition to the CRC screening armamentarium, I believe it will be a useful additional option rather than a stand-alone panacea.

To appreciate the potential role of noncathartic CT colonography for CRC screening, one must consider the advantages and disadvantages relative to CT colonography using a cathartic preparation. The major advantage of a laxative-free approach is the potential for an overall increase in screening compliance, particularly from those seeking to avoid cathartic preparation. Unfortunately, I believe there are a host of caveats (discussed subsequently) that may temper the actual benefit in both increased participation and effective resource use. Nonetheless, even a relatively small marginal gain in compliance represents another step in the right direction that should be embraced. Another advantage to a laxative-free approach is avoidance of the risks associated with purgative preparation. This is particularly important for patients with known or undisclosed risks factors, such as renal or cardiac insufficiency.

See also page 666

On closer inspection, there are a number of relative disadvantages to screening with noncathartic CT colonography that may ultimately relegate it to a useful but secondary option compared with the current cathartic approach. Potential drawbacks worthy of further consideration include the following: (1) current laxative-free regimens are far from being "prepless"; (2) the potential negative impact on accuracy could lead to both missed lesions and overuse of colonoscopy; (3) the lack of cathartic preparation precludes same-day therapeutic colonoscopy; (4) the greatest aversion to cathartic preparation appears to be from those who have already been screened; and (5) cumulative experience with cathartic preparations suggests a favorable safety profile. Many discussions surrounding a laxative-free approach to CT colonography use the term *prepless*, which unfortunately represents a euphemistic misnomer since it implies that no intervention or steps are necessary leading up to the examination. On the contrary, most noncathartic preparations for CT colonography involve a fairly rigorous regimen that consists of both dietary restriction and ingestion of various oral contrast agents.[2-4] Because of the cathartic-like effect of oral

Dr Pickhardt is a consultant for Fleet Pharmaceuticals.

Address correspondence to Perry J. Pickhardt, MD, Department of Radiology, University of Wisconsin Medical School, E3/311, Clinical Science Center, 600 Highland Ave, Madison, WI 53792-3252 (e-mail: pj.pickhardt@hosp.wisc.edu).

contrast agents such as diatrizoate, use of the terms *noncathartic* or *minimal prep* is questionable. Such noncathartic preparations may also extend for 48 hours or longer, perhaps resulting in a process that is equally or even more onerous than some low-volume cathartic regimens currently in use.[5] Beebe et al wisely avoid using the term *prepless*. However, one major flaw of the survey is that respondents were likely equating "laxative-free" with "prepless," which is clearly not the relevant comparator given the current status of noncathartic CT colonography. Preference for actual noncathartic vs cathartic preparations will need to be assessed before attaching any real value to removal of the laxative.

Because residual stool is widely recognized as a major source of potential error at CT colonography,[6-8] the effect of a laxative-free approach on polyp detection accuracy is an important concern. The use of oral contrast agents for tagging residual stool and fluid will reduce both false-positive and false-negative results somewhat but will certainly not eliminate them. Any additional false-positive results caused by withholding the laxative would lead to unnecessary colonoscopy, which is not only inconvenient and lacks benefit but also leads to higher costs and increased procedural risks. Perhaps the greatest concern is that even a moderate amount of residual adherent stool largely reduces polyp detection at CT colonography to a primary 2-dimensional (2-D) search since 3-D evaluation is generally not feasible because of the large number of 2-D correlations needed. Unfortunately, CT colonography with primary 2-D polyp detection has proved to be an inadequate approach in screening cohorts with a low prevalence of polyps,[9,10] whereas primary 3-D evaluation has performed well.[11] At the very least, any laxative-free approach to CT colonography must first be validated in a large multicenter trial before being applied for asymptomatic screening.

From a practical standpoint, even the detection of true-positive large polyps with noncathartic CT colonography leads to a major inconvenience for patients by requiring a full cathartic preparation on a separate day, followed by optical colonoscopy the following day. In our experience, patients clearly value the "1-stop shop" approach of same-day polypectomy provided by our screening program, whereby CT colonography with a cathartic preparation virtually guarantees that only 1 bowel preparation is needed.[5] For every false-positive interpretation at noncathartic CT colonography that leads to a negative (and ultimately unnecessary) colonoscopy, the chances are good that a cathartic preparation with stool tagging could have avoided the extra test, since our current positive predictive value for concordant findings at colonoscopy is approximately 90%.[5]

The survey results from Beebe et al found that those who had previously undergone screening had the greatest aversion to a laxative preparation. However, the most important screening subset is the majority of adults who have never been tested. Because of the high negative-predictive value of CT colonography screening that exceeds 99%, exclusion of clinically relevant polyps places an individual in a very low-risk category. Given the limited resources available for population screening and the unwillingness of patients to adhere to recurrent screening regimens, the utility of 1-time screening deserves consideration.[12] A 1-time screening model diminishes the importance of the survey findings among those who were previously tested.

The safety profile to date for cathartic preparations for CT colonography has been favorable. In our experience dating back to the screening trial, we have witnessed no major prep-related complications in more than 5000 patients, including use of sodium phosphate in more than 4000 cases. However, because of rare reported instances of acute phosphate-induced nephropathy, we avoid the use of sodium phosphate in elderly patients with hypertension, particularly those taking angiotensin-converting enzyme inhibitors, as well as patients with renal or cardiac insufficiency.[13] We have found that a single 45-mL dose of sodium phosphate is equally effective as a double dose, which complies with the Food and Drug Administration labeling.[14]

Computed tomographic colonography has the potential to revolutionize CRC screening in the very near future. Because increased participation in effective screening programs represents the overriding challenge facing CRC prevention, offering both cathartic and noncathartic options for CT colonography may very well be the most prudent approach for our heterogeneous population that expresses divergent preferences and needs. Although it may initially appear counterintuitive, the noncathartic approach to CT colonography may in fact turn out to be more onerous overall than a low-volume preparation that incorporates laxatives, especially for patients with positive findings on examination.

Perry J. Pickhardt, MD
Department of Radiology
University of Wisconsin Medical School
Madison

1. Beebe TJ, Johnson CD, Stoner SM, Anderson KJ, Limburg PJ. Assessing attitudes toward laxative preparation in colorectal cancer screening and effects on future testing: potential receptivity to computed tomographic colonography. *Mayo Clin Proc*. 2007;82:666-671.

2. Callstrom MR, Johnson CD, Fletcher JG, et al. CT colonography without cathartic preparation: feasibility study. *Radiology*. 2001;219:693-698.

3. Lefere PA, Gryspeerdt SS, Dewyspelaere J, Baekelandt M, Van Holsbeeck BG. Dietary fecal tagging as a cleansing method before CT colonography: initial results—polyp detection and patient acceptance. *Radiology.* 2002;224:393-403.

4. Iannaccone R, Laghi A, Catalano C, et al. Computed tomographic colonography without cathartic preparation for the detection of colorectal polyps. *Gastroenterology*. 2004;127:1300-1311.

5. Pickhardt PJ, Taylor AJ, Kim DH, Reichelderfer M, Gopal DV, Pfau PR. Screening for colorectal neoplasia with CT colonography: initial experience from the 1st year of coverage by third-party payers. *Radiology.* 2006 Nov; 241:417-425. Epub 2006 Sep 18.

6. Macari M, Bini EJ, Jacobs SL, Lange N, Lui YW. Filling defects at CT colonography: pseudo- and diminutive lesions (the good), polyps (the bad), flat lesions, masses, and carcinomas (the ugly). *Radiographics.* 2003;23:1073-1091.

7. Pickhardt PJ. Differential diagnosis of polypoid lesions seen at CT colonography (virtual colonoscopy). *Radiographics.* 2004;24:1535-1556.

8. Pickhardt PJ, Choi JR. Electronic cleansing and stool tagging in CT colonography: advantages and pitfalls with primary three-dimensional evaluation. *AJR Am J Roentgenol.* 2003;181:799-805.

9. Cotton PB, Durkalski VL, Pineau BC, et al. Computed tomographic colonography (virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colorectal neoplasia. *JAMA.* 2004;291:1713-1719.

10. Rockey DC, Paulson EK, Davis W, et al. Multicenter prospective comparison of colon imaging tests. Presented at: Digestive Disease Week; May 15-20, 2004; New Orleans, La.

11. Pickhardt PJ, Choi JR, Hwang I, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. *N Engl J Med.* 2003 Dec 4;349:2191-2200. Epub 2003 Dec 1.

12. Ness RM, Holmes AM, Klein R, Dittus R. Cost-utility of one-time colonoscopic screening for colorectal cancer at various ages. *Am J Gastroenterol.* 2000;95:1800-1811.

13. Pickhardt PJ. Screening CT colonography (virtual colonoscopy): how I do it. *AJR Am J Roentgenol*. In press.

14. Kim DH, Pickhardt PJ, Hinshaw JL, Taylor AJ, Mukherjee R, Pfau PR. Prospective blinded trial comparing 45-mL and 90-mL doses of oral sodium phosphate for bowel preparation prior to computed tomographic colonography. *J Comput Assist Tomogr.* 2007;31:53-58.