Published in final edited form as:

Acad Radiol. 2009 July ; 16(7): 777–779. doi:10.1016/j.acra.2009.04.001.

The Elephant in the Room: Bowel Preparation for CT Colonography Editorial for Academic Radiology article 08410R1

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CT colonography (CTC), also known as virtual colonoscopy, is entering a new era. With the recent publication of the successful ACRIN National CT Colonography Screening Trial, CTC is now widely recognized as a highly sensitive and specific test for identifying polyps in the colon (1). Attention is now turning towards reimbursement, training and dissemination of the technique into community practices. Negative issues such as the costs of workup of extracolonic findings and the potential harms of the radiation dose are now under investigation. But there is one “elephant in the room” that is mentioned less often: the poor patient acceptance of the bowel preparation common to both optical and virtual colonoscopy (2-4).

In this issue of Academic Radiology, Nagata and colleagues prospectively compared CTC in high-risk patients using two different bowel preparations, a full standard laxative preparation and a “minimum preparation” with reduced laxative administration. The patients were a consecutive series of 101 subjects who were alternately assigned to either preparation. Within seven days the minimum preparation patients also underwent optical colonoscopy after a full bowel preparation and hence received both preparations. Both preparations included tagging of residual fluid and feces with inexpensive sodium diatrizoate. Results of a questionnaire given to the patients indicated a strong preference and high tolerance for minimum preparation CTC over colonoscopy. Both bowel preparations led to high sensitivity for detecting polyps 6 mm or larger (97% for the full preparation and 88% in the minimum preparation) but the specificity was much lower for the minimum preparation group (92% versus 68%, respectively). The quality of fecal tagging was also poorer in the minimum preparation group. Nevertheless, the authors concluded that because of its high sensitivity and patient acceptance, patients should be offered the minimum laxative version of CTC as an alternative to full laxative preparation if they were willing to accept the decrease in specificity.

Bowel preparation has been an important subject of CTC research over the past decade. The earliest preps mimicked those used in barium enema and colonoscopy, typically a vigorous cathartic cleansing with oral bisacodyl tablets and two to four liters of polyethylene glycol (PEG) (5-7). Researchers soon began exploring other bowel preparations. An early successful choice was a switch to oral sodium phosphate preps which were shown to leave less residual fluid in the colon (8). Soon thereafter, iodine- and/or barium-containing oral contrast agents

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Potential financial interest. The author has pending and/or awarded patents and receives royalty income and grant support from iCAD Medical. He received free research software from Viatronix.

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were added to the sodium phosphate preparation and shown in a seminal multi-institutional clinical trial to lead to high sensitivity and patient acceptance of CTC (9). The oral contrast agents improved sensitivity for polyp detection by tagging residual fecal matter and colonic fluid. At about the same time, researchers began investigations of CTC without a cathartic preparation (10-12) or with less vigorous cleansing using dietary modification and oral administration of various combinations of magnesium citrate, bisacodyl, senna, diatrizoate meglumine and barium (10,13-15).

The laxative-free and reduced cleansing CT colonography bowel preps made it more challenging to interpret the images because polyps were hard to see in the presence of incompletely tagged stool and residual fluid. Subsequently, researchers developed "electronic cleansing" to identify and remove residual fluid and/or fecal matter from the CTC images (16-24).

Despite the advances in electronic cleansing and the hope that laxative-free or minimal preparation CTC will be successful, full preparation is considered the clinical standard now that the ACRIN trial proved its efficacy. Nagata et al. have challenged the need for a full prep with CTC by showing high sensitivity for polyp detection with minimum preparation CTC. Moreover, since Nagata and colleagues did not use electronic cleansing, whether electronic cleansing would have improved the results is unknown. Another factor to consider is the patient population. The subjects in Nagata's study were relatively young, with mean ages of about 55 years. Older patients may not cleanse as well and could have poorer sensitivity for polyp detection.

However, a problem remains: the 24% decrease in specificity in the minimum preparation group compared to the full preparation group. Thus, about one quarter more of the subjects without polyps would be referred for an unnecessary optical colonoscopy based on false positive findings at minimum preparation CTC. Would patients accept such a high false positive rate if they were told about it beforehand? Would physicians be willing to refer patients for an examination in which about one third of normal subjects (based on 68% specificity) needed to undergo two tests (optical and virtual colonoscopies) instead of just one? Not only would the patients undergo two tests, but they would undergo two expensive tests as well as a full cathartic preparation. It seems highly unlikely that medical advisory bodies and payors would look favorably upon this situation.

The authors correctly state that an important objective of future research is a better, more acceptable minimum preparation. What would such a preparation look like? To achieve the desired goal, investigators need to ask the right questions. Many studies have shown that patients don't like the preparation but few have fully analyzed the problem. What is it about the preparation that patients don't like? Is it the experience of drinking the preparation (i.e., flavor, saltiness, volume, viscosity), the side effects (number of trips to the bathroom, diarrhea, abdominal pain, cramping, sleep deprivation), or the logistics (complexity, scheduling or duration, dietary modifications, convenience of obtaining), or combinations of the above? These are important issues if we are to develop a patient friendly and accurate minimum preparation CT colonography. We need a rigorous analysis of all the relevant factors to improve compliance and acceptability and decrease avoidance of screening. The authors' preparation involved ingestion of sodium picosulfate, a cathartic, and sodium diatrizoate, a tagging agent that is also a mild cathartic. The tagging was given over a three day interval while the patients were on a low fiber diet. Perhaps additional doses of sodium picosulfate would improve the bowel cleansing without reducing patient acceptance.

It seems clear that the large volume bowel preps such as that used in the full preparation are unacceptable to many patients. In one survey of patients undergoing both CTC and optical

colonoscopy, the bowel preparation was the worst part of either test, and drinking the fluid was the worst part of the bowel preparation, ahead of the unpleasantness of the liquid diet or frequent trips to the bathroom (25). Of note, the majority of the patients in that study used the low volume sodium phosphate preparation. A low volume cathartic CTC preparation was preferred to a higher volume optical colonoscopy preparation in a head-to-head comparison (26). A “lower” volume cathartic preparation with 75 ML of sodium phosphate compared to 90 ML for colonoscopy achieved higher patient acceptance and increased willingness to repeat the preparation for a future examination (27). Of note, this study was sponsored by the company that produces the sodium phosphate preparation. A study of optical colonoscopy showed a 2 L PEG preparation with ascorbic acid was more acceptable to patients than a 4 L PEG preparation with electrolytes (28). The ascorbic acid improves the taste and has an osmotic effect, allowing the amount of PEG to be reduced. Is it really necessary to give even 2 L of PEG? Perhaps 1 L would suffice.

Is the key to use a more powerful cathartic or a lower volume one or both? Sodium phosphate has been used in many full preparations for CTC and its volume is quite small, only about 45 ML, perhaps explaining its high acceptability by patients. However, sodium phosphate requires more care in its administration because it is contraindicated in patients with reduced renal function. Would a 20 ML sodium phosphate preparation be adequate? There is little research in this area.

Could enemas be part of the preparation? The authors did not analyze the locations of the false negatives and false positives by colonic segment. If these were predominantly distal, a saline and iodine enema prior to CTC could be a solution but would certainly complicate the procedure and reduce patient acceptability.

Bowel preparation is a key component of both a high performing and acceptable colorectal cancer screening test. Image processing, including computer-aided polyp detection (CAD), is likely to be part of the solution but even the best CAD will fail with inadequate bowel preparation. If we can get the bowel preparation for CTC right, patients will be more likely to undergo screening. The best minimum or non-cathartic preparation for CT colonography remains to be found.

Acknowledgments

The author thanks Andrew J. Dwyer, MD, and Marius Linguraru, PhD, for critical review of the manuscript. This work was supported by the Intramural Research Program of the National Institutes of Health Clinical Center.

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