Computed Tomography Colonography for Colorectal Cancer Screening

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Abstract: Colorectal cancer screening has been shown to help prevent cancer-related death. Concerns about suboptimal adherence to conventional colonoscopy has led to the search for alternative screening modalities. Computed tomography colonography (CTC) is a highly sensitive and minimally invasive alternative modality. The American College of Radiology has established a standardized reporting system for CTC. The advantages of CTC include complete colonic examination and extraluminal imaging in a single breath hold time. Lack of sensitivity in the evaluation of flat lesions and radiation exposure are the main concerns with this modality. Although the usefulness of CTC has been demonstrated in academic centers, larger studies in community settings are needed to facilitate its adoption by healthcare services.

Keywords
Colorectal cancer, computed tomography colonography, optical colonoscopy

Colorectal cancer (CRC) is the third most common cancer and second leading cause of cancer death in the United States, with nearly 150,000 new cases each year.[1] CRC usually evolves from a small lesion by a series of mutations. With time, it transforms into a large adenomatous polyp that transforms into cancer within an average of 5.5 years.[2] This slow growth provides a window of opportunity for screening and intervention.

It is estimated that 60% of CRC-associated deaths could be prevented if all individuals 50 years of age and older underwent CRC screening.[3] However, only 64.2% of adults older than age 50 years adhere to the current CRC screening guidelines with the use of optical colonoscopy (OC).[4] Because of this, alternative screening options are being explored.

Colorectal Cancer Screening Tests

There are 2 categories of screening tests for CRC prevention: stool-based tests (guaiac and immunochemical fecal occult blood tests and fecal DNA tests), which are sensitive to the detection of CRC but not polyps, and structural/imaging tests (sigmoidoscopy, OC, double-contrast barium enema [DCBE], computed tomography colonography [CTC], capsule colonoscopy, and magnetic resonance

[MR] colonoscopy), which are capable of detecting both CRC and polyps.[5] CTC is superior to DCBE.[6] Although OC is the current gold standard screening test, CTC as well as capsule colonoscopy and MR colonoscopy are potential alternatives to OC. This review focuses on CTC.

CTC was developed in 1994.[7] It is relatively less invasive than conventional colonoscopy and does not require anesthesia, although it requires colon preparation and rectal catheter insertion. Because its image acquisition time is approximately 15 seconds, it has been better accepted by the general population than OC.[8] It has been suggested that CTC may be used as a triage tool for OC in patients at low to medium risk for CRC, such that they would be screened with CTC and then subjected to OC only if a polypectomy is required.[9] When OC is not successful due to technical reasons or it cannot be performed because of the risk of complications, such as in patients who receive anticoagulation therapy or who have significant pulmonary disease, CTC may serve as an alternative for the complete imaging of the colon.

Target Lesions

The crucial test for a structural/imaging examination is the ability to detect clinically significant target lesions for the potential to progress to CRC. These lesions are tubular adenomas greater than 1 cm, adenomas with high-grade dysplasia or significant villous components, or invasive cancer.[10-12]

Until imaging markers indicative of histology are developed, polyp size will remain the most important factor in determining the management of colonic polyps. The absolute prevalence of advanced adenomas, according to a recent study,[13] was 0.3% for polyps smaller than 6 mm, 0.4% for polyps 6–9 mm, and 4.9% for polyps larger than 9 mm. The study authors estimated that a 6-mm polyp threshold for polypectomy referral would identify over 95% of advanced adenomas, whereas a 10-mm threshold would identify 88%. At present, however, a debate persists concerning the size threshold for referral for polypectomy. The joint recommendation of the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology states that patients with polyps greater than 6 mm should be offered polypectomy.[14] The 2005 guidelines from the American College of Radiology proposed reporting and data system category recommendations, which remain the current standard (Table).[15]

Most CTC studies have not reported polyps smaller than 6 mm, as per the policy of the American College of Radiology.[15] The 3 reasons for this policy are: (1) The incidence rates of cancer and high-grade dysplasia in polyps in this size range are much lower (<1%) than those of polyps 6 mm or larger, and villous elements are uncommon.[16] (2) Most of these polyps have hyperplastic histology and, hence, are soft in consistency, which favors their effacement against the colonic mucosa once the colon is inflated, resulting in nonvisualization.[17] (3) Reporting insignificant polyps, as a defensive practice, may lead to unnecessary referral to OC for polypectomy, adding to the cost of care and potential procedure-related complications.

Table. Colonography Reporting and Data System Categories

Category	Diagnosis	Recommendation
C0	Inadequate study/awaiting comparisons	Obtain comparisons
C1	Normal colonic or benign lesion: no polyp ≥6 mm	Routine screening every 5–10 years
C2	Indeterminate polyp(s) or finding(s): one or two 6–9-mm confirmed or possible polyp(s)	CTC surveillance or OC
C3	Possibly advanced adenoma: ≥1 polyp(s) ≥10 mm or three or more 6–9-mm polyps	OC
C4	Colonic mass: likely malignant	Surgical consultation

CTC=computed tomography colonography; OC=optical colonoscopy.

Sensitivity

Multiple studies have been performed to determine the sensitivity of CTC for polyp detection. In 2005, a meta-analysis by Mulhall and colleagues stated that CTC is highly specific but has a very wide range of sensitivities.[18] A great deal of heterogeneity exists in terms of population studied, CT equipment, software, radiation exposure, data acquisition, image processing, reference standards for assessing CTC sensitivity, bowel preparation, protocols, colonoscopes, number of readers, and level of experience of radiologists and endoscopists in the studies performed so far. Studies that used consensus or multiobserver readings[19] may not be representative of what is typical and may have increased bias.

Overall, a sensitivity of more than 90% for polyps over 10 mm was found in various studies, although marked heterogeneity was seen in terms of population size, type of cohort studied, and technique used (including techniques using minimal bowel preparation[20] and reduced radiation exposure).[21-23] Early studies examined patients at high risk for colonic abnormalities.[24-27] Most later studies also were performed in cohorts at high risk,[28-30] although a few prominent studies examined

average-risk populations.[31-33] Recently, Pickhardt and colleagues conducted a meta-analysis to evaluate the efficacy of CTC compared with OC for screening of CRC.[34] They reported a sensitivity rate of 96.1% for CTC compared with a rate of 94.7% for OC for cancer detection.

Protocols

Imaging with dual patient positioning (supine and prone) is used for fluid and stool redistribution as well as improvement in segmental distention. The routine use of spasmolytics is controversial because peristalsis is intermittent or of low amplitude and the motion artifacts due to peristalsis are relatively rare and, as such, their use is advocated mainly to improve patient comfort.[35,36]

A properly cleansed colon maximizes the ability to differentiate polyps from folds and residual stool and minimizes false-positive results.[37] The most common bowel preparation prescribed is polyethylene glycol solution plus bisacodyl. Sodium phosphate is no longer used because of the risk of phosphate nephropathy. Magnesium citrate is now also being used with good results.[38] Residual colonic fluid and stool can obscure a large portion of the colon wall and hide polyps. Using barium for stool tagging, diatrizoate meglumine for fluid tagging, and digital subtraction of residual fluid and stool are useful for overcoming this problem.[39]

Both two-dimensional (2D) and three-dimensional (3D) imaging have been used for CTC. Visualization of lesions, internal heterogeneity, lesion density, and wall characteristics are better depicted by the transverse 2D image because of its capability to depict wall characteristics and pericolonic structures along with the target polyp, making cancer detection possible for even small lesions.[39] External morphologic features of the lesions are better captured by the 3D view because it has the ability to display the entire endoluminal surface (both sides of folds), making it more sensitive for detecting smaller lesions.[40]

A prospective study by Pickhardt and colleagues[41] concluded that primary 3D polyp detection via CTC is superior to the standard primary 2D approach for low-prevalence screening. Primary 2D CTC sensitivity for adenomas 6 mm or larger was 44.1% compared with 85.7% with 3D. Nevertheless, supplementary 2D evaluation can be useful in cases with abundant adherent stool or areas of partial or total luminal collapse. 2D evaluation is also useful for accurate dismissal of false-positive lesions.

Merits

CTC also can evaluate the proximal colon when OC is incomplete, as in the case of an obstructive lesion. There are no blind areas, such as the opposite side of the colonic fold, on a "hairpin" bend, or at the anal verge, where colonoscopy has a high propensity to miss a lesion. Pickhardt and colleagues found that 10.8% of polyps 5 mm or larger identified by OC among 1,233 asymptomatic adults who underwent same-day OC and CTC were identified only after a second-look OC following segmental unblinding of CTC results.[42] Also, evaluation of the right colon is technically more difficult than that of the left colon during OC. With CTC, evaluation of the right colon is easier than the left and sigmoid colon because distention is better.[43]

With multidetector helical CT, imaging of the abdomen and pelvis can now be accomplished in a single breath hold, eliminating most respiratory and bulk body motion artifacts. Slice thicknesses determine the size of a lesion, which can be detected by CTC and need to be 3 times smaller than the target size of the lesion to overcome the variable obliquity of colonic segments.[44] The widespread use of collimations smaller than 2.5 mm and reconstruction intervals of 1.25 mm or smaller for CTC has highly enhanced the ability to detect polyps larger than 5 mm.[45]

CTC can provide insight into the natural history of polyps, offering improved anatomic location, compared with OC, and precise size estimation of polyps for longitudinal follow-up with both intraluminal and extraluminal registration.[46] In addition, the computer processing power and 3D CTC software have resulted in an improved computer-aided diagnosis that may have the potential to reduce interpretation time and error rates due to reader fatigue after viewing multiple examinations.[47-49]

CTC also has the potential to diagnose clinically significant extracolonic findings. The prevalence of identifying extracolonic findings of moderate potential importance ranges from 7.4–11.4%.[50,51] In a recent study of routine CTC screening for CRC in asymptomatic healthy adults, clinically unsuspected cancer was detected with a frequency of greater than 1 case per 200 individuals screened.[52] However, there is a concern for the risks and costs associated with false-positive and inconsequential findings.[53] Potential harms include the anxiety, inconvenience, potential complications, unnecessary surgery, and added costs related to the additional diagnostic work-up for findings that ultimately prove to be unimportant.[54,55] It has been suggested that the usefulness of CTC may be enhanced when the detection of extracolonic cancers and aortoiliac aneurysms is included along with CRC screening.[55]

In addition to technical advantages, CTC has a better acceptance among patients. Pooler and colleagues conducted a multicenter survey involving 1,417 patients to evaluate patient experience and satisfaction with CTC screening and compare preference with screening colonoscopy.[56] These investigators found that CTC, if widely available, has the potential to increase adherence to CRC screening guidelines. Stoop and colleagues compared the

participation and diagnostic yield of screening with OC with those of noncathartic CTC and reported significantly better participation with CTC.[57]

Complications

An associated perforation rate of between 0.06% and 0.08% has been reported with CTC[58,59] and is further estimated to be lower in an average screening population.[60] This compares well with diagnostic colonoscopy, which has an associated perforation rate of 0.1–0.2%.[61] Caution is needed in interpretation; CTC overestimates perforations because of the much higher sensitivity of CT in the detection of even tiny air bubbles. The mere finding of extraluminal gas at CTC is distinct from a symptomatic perforation. Likewise, asymptomatic right-sided colonic pneumatosis (ie, air in the bowel wall) also is a rare but benign imaging finding associated with CTC and should not be confused with symptomatic perforation.[62] Most of the perforations reported in a UK survey were treated conservatively, without surgical intervention.[58] Nevertheless, the use of soft rectal catheters and colonic distention with low-pressure CO_2 delivery can further reduce the rate of perforations.[63]

Radiation exposure is one of the concerns for large-scale use of CTC for CRC screening. The estimated risk of cancer induced by radiation as a result of a CTC study is 0.14% in a patient 50 years of age.[64] A position statement issued by the Health Physics Society states that the health effects of low-dose radiation (defined as 50 mSv) are considered "either too small to be observed or are nonexistent."[65] In a recent survey of research institutions performing CTC, Liedenbaum and colleagues found that the median effective dose for a screening CTC was 5.8mSv (or 2.5–2.8 mSv per position).[66] For a radiation dose of approximately 5–8 mSv at 50 years of age, the lifetime risk of death from cancer varies between 0.02% and 0.03%.[67] Thus, the impact of radiation caused by CTC examinations appears insignificant. However, additional studies, preferably prospective long-term observational studies, are now needed to answer this important question. Radiation dose during CTC can be reduced to 50% below currently accepted low-dose techniques without significantly affecting image quality when adaptive statistical iterative reconstruction is used.[68]

Technical Pitfalls

One of the concerns about CRC screening is the prevalence of flat polyps, for which CTC has not been found to be very sensitive. Although several studies have addressed the prevalence of flat lesions, definitive conclusions regarding their importance are lacking.[69-72] However, in a recent study involving 5,107 patients in a US screening population, it was found that flat colorectal lesions detected on CTC demonstrated less aggressive histologic features compared with polypoid lesions.[17]

There is a possibility of missing rectosigmoid cancers during CTC due to the presence of an inflated rectal balloon and enema tube and challenges with luminal distention.[73] The regions around the ileocecal valve and anus are susceptible to anatomic distortion on virtual imaging. Annular constricting or infiltrating masses also can be difficult to detect because these lesions occlude the lumen and can lead to a gap in the virtual dissection image.[74] Orthopedic hardware, such as hip arthroplasty devices, also can severely limit the usefulness of CTC in the pelvis, which requires metal artifact suppression software to improve the image quality.[75]

Colonic or pedunculated mobility can change the morphology of polyps, which can lead to mischaracterization of the polyp as mobile stool.[76] Polyps located on folds may be difficult to detect if there are adjacent distorted folds; they can be overlooked as part of normal fold distortion. Diverticulae on virtual images often have the same appearance as polyps; hence, correctly identifying polyps in the setting of diffuse diverticulosis can be difficult. Stool may mimic a polyp if it adheres to the colonic wall. Other sources of false-positive lesions are non-neoplastic anorectal lesions, ileocecal valve variants, inverted appendiceal stumps, and submucosal and extrinsic lesions.[77]

Reimbursement Issues

CTC has been endorsed by the American Cancer Society and US Multi-Society Task Force, but the US Preventive Services Task Force states that there are insufficient data to recommend CTC screening for the average-risk population.[14,78,79] The Asia Pacific Working Group on Colorectal Cancer and the American College of Gastroenterology consider CTC a second-line screening test for those unwilling or unable to undergo OC and those in whom OC was incomplete.[5,80] The largest US healthcare service, Medicare, still denies reimbursement of screening examinations performed with CTC.[81] However, it has recently been reported that national and regional trends in Medicare coverage of diagnostic CTC by fee-for-service beneficiaries has tripled.[82] More than half of all examinations are now reimbursed, despite perceptions among physicians that new technology tracking codes are not payable.

Conclusions

The American College of Radiology has now established preliminary quality metrics in colonography in an effort

to establish benchmarks for the quality of CTC examinations. The College concluded that CTC will continue to further transition into community practice and can provide an important adjunctive examination for CRC screening.[83] Technological improvements to minimize radiation exposure should continue while monitoring long-term effects. Continued efforts to simplify and minimize bowel preparation are essential to CTC's success and may improve compliance, as bowel preparation is one of the greatest barriers to CRC screening. The CTC technology needs to be evaluated beyond academic centers, preferably in the large-scale community practice environment.

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