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EDITORIAL

Computed tomographic colonography: Hope or hype?

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Abstract

Computed tomographic colonography (CTC) is a promising emerging technology for imaging of the colon. This concise review discusses the currently available data on CTC technique, test characteristics, acceptance, safety, cost-effectiveness, follow-up strategy, and extracolonic findings. In summary, CTC technique is still evolving, and further research is needed to clarify the role of automated colonic insufflation, smooth-muscle relaxants, intravenous and oral contrast, software rendering, and patient positioning. Currently, full bowel preparation is still required to achieve optimal results. The sensitivity for detecting large polyps (> 1 cm) can be as high as 85%, with specificity of up to 97%. These test characteristics are almost comparable to those of conventional colonoscopy. Patient acceptance of CTC is generally higher than that for colonoscopy, especially in patients who have never undergone either procedure. CTC is generally safe, although uncommon instances of colonic perforation have been documented. In terms of cost-effectiveness, most decision analyses have concluded that CTC would only be cost-effective if it were considerably cheaper than conventional colonoscopy. The proper follow-up strategy for small polyps or incidental extracolonic findings discovered during CTC is still under debate. At present, the exact clinical role of virtual colonoscopy still awaits determination. Even though widespread CTC screening is not available today, in the future there may eventually be a role for this technology. Technological advances in this area will undoubtedly continue, with multi-detector row CT scanners allowing thinner collimation and higher resolution images. Stool-tagging techniques are likely to evolve and may eventually allow for low-preparation CTC. Perceptual and fatigue-related reading errors can potentially be minimized with the help of computer-aided detection software. Further research will define the exact role of this promising technology in our diagnostic armamentarium.

Key words: Computed tomographic colonography; Colonoscopy; Colonic neoplasms; Cancer screening; Colonic polyps

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INTRODUCTION

First described in 1994[1], virtual colonoscopy, more properly termed computed tomographic colonography (CTC), uses dedicated processing software to generate 2- and 3-D reconstructions of the colon and rectum, based on data obtained by high-definition CT of the abdomen and pelvis. In recent years, there have been rapid advances in this technology, heightening its potential as a less invasive means of visualizing the colon. However, there remain numerous pitfalls to its widespread use. This article gives a succinct review of CTC technique, test characteristics, acceptance, safety and cost-effectiveness, to give an informed understanding of the potential of this promising new imaging modality.

TECHNIQUE

CTC technique is constantly evolving, and there is still considerable variation depending on institutions. Currently, in most facilities, a full bowel preparation is required for CTC because retained stool cannot be reliably differentiated from polyps. The colon is distended with gas during the scan, as visualization is compromised in underinflated segments. The degree of insufflation may be controlled by the technician, the patient or an automated insufflation device. In most centers, room air is used for colonic distension, but carbon dioxide may be better tolerated because it diffuses through the colonic wall more quickly[2]. Smooth-muscle relaxants can theoretically reduce artifacts from colonic motility[3], while the use of intravenous contrast may result in better differentiation of polyps from colonic fluid[4]. In addition, oral iodinated contrast can be ingested to change the attenuation of residual colonic fluid; however, studies have not demonstrated any significant improvement in accuracy[5].

During colonography, the abdomen is scanned during one or two breath-holds that last < 2 min. Scans are performed in the craniocaudal direction, with the patient in the prone and supine positions. The incorporation of the prone position has been shown to improve distension of colonic segments and allow for displacement of fluid and stools[5]. Studies have suggested that scanning in the supine and left lateral decubitus positions improves visualization even further[6]. The best results for CTC require the use of multidetector (4-8 channels) scanners with 1.25-2.5 mm collimation, and reconstruction intervals of 1 mm. Standard helical images of the colon are processed by imaging software using one of three rendering techniques: surface rendering, volume rendering, or perspective rendering. In addition to 2-D axial, coronal and sagittal images, 3-D rendered views of the colon that simulate endoluminal views during colonoscopy can be reproduced. These allow both anterograde and retrograde "fly throughs" of the colon, with the ability to examine the proximal aspect of the haustral folds, a potential blind spot for conventional colonoscopy.

TEST CHARACTERISTICS

Ever since publication of the initial study on the sensitivity and specificity of CTC compared to conventional colonoscopy[7], numerous studies have reported widely disparate estimates of CTC test performance, probably due to differences in examination techniques, patient populations, reference standards, and examiner experience or skill. Many of the earlier studies used single-row scanners and showed mediocre or poor CTC sensitivity, especially for small polyps. More recent studies have used multi-detector scanners and have adopted more rigorous study designs, and some have reported favorable test performance characteristics. The results of the six largest studies to date in western populations are as follows.

In 2003, Pickhardt *et al*[8] presented a landmark study that showed that, under optimal conditions, CTC had comparable sensitivity and specificity to conventional colonoscopy. For detecting large polyps ≥ 10 mm in size, the sensitivity of CTC was 92%; for smaller polyps (≥ 6 mm), the sensitivity was 86%. In this study, the investigators achieved excellent results by performing solid-stool tagging with oral barium and opacification of colonic fluid with iodinated contrast, post-procedure "electronic cleansing" with software that digitally removed opacified colonic fluid, and primary reading of 3-D images, with 2-D images used for problem solving. Segmental unblinding was adopted to provide an enhanced gold standard, and indeed CTC detected several lesions that were missed by conventional colonoscopy, as described by the authors in a follow-up study[9]. More recently, the multicenter ACRIN study, which featured the largest sample size to date (2531 subjects), reported a sensitivity of 90% and specificity of 86% for large polyps[10], while another study on 1103 Italian patients achieved a sensitivity of 85% and specificity of 87% for advanced neoplasia[11]. However, three other large studies have reported less impressive results, with sensitivities of 63%, 55% and 59% for the detection of large polyps (≥ 10 mm)[12-14]. Large-scale CTC screening has also been used in Asian populations, with variable degrees of success[15,16].

Four meta-analyses have been published to summarize the available data. An earlier meta-analysis that involved 14 studies reported a pooled sensitivity of 81% for large polyps (≥ 10 mm) and 43% for small polyps (≤ 5 mm)[17], while another meta-analysis of 24 studies reported a sensitivity of 93% for large polyps[18]. These two reviews did not include many of the more recent studies. A subsequent, more comprehensive meta-analysis included 33 studies (comprising a total of 6393 patients), and calculated pooled sensitivities ranging from 48% for small polyps (≤ 5 mm) to 85% for large polyps (≥ 10 mm). Specificity was more consistent, between 92% and 97%[19]. The most recent meta-analysis included 30 studies and used a summary receiver operating characteristic method for combining data, and reached similar conclusions[20].

Technical factors that can limit the accuracy of CTC include poor bowel preparation, inadequate colonic distension, breath-hold artifacts and suboptimal image resolution. The sigmoid colon is often a problematic area, although diverticulosis does not appear to adversely affect the accuracy of CTC[21]. The rectum is another site with high miss rates for polyps because it is difficult to achieve adequate air insufflation there[2,22]. Studies have now confirmed that flat adenomatous lesions are common in western patients, and many of these may feature advanced neoplastic histology[23]. Such flat lesions may be difficult to recognize on CTC. Perceptual failure, when the polyp is evident on the scan but is not recognized as such by the reader, is thought to be correlated with inadequate training, limited experience and reader fatigue[24].

PATIENT ACCEPTANCE

At present, it is unclear if patients find CTC preferable to colonoscopy. In general, colonoscopy is perceived as being more invasive. However, colonoscopy offers the advantage of a "one-stop" diagnostic and therapeutic procedure, and its discomfort is mitigated by the use of conscious sedation in most developed countries. We recently presented data on a systematic review and meta-analysis on patient acceptance of CTC compared with conventional colonoscopy[25]; we reviewed 19 studies and found that, in general, patients preferred CTC over colonoscopy, although there was significant heterogeneity between studies (risk difference of 24%, $P < 0.001$). Bowel preparation is universally perceived as the worst part of both procedures. There have been efforts to improve the accuracy of low-dose bowel preparation CTC[26-31]. If this becomes a commonly available procedure, patients will likely find CTC much more acceptable.

SAFETY

CTC may not be as free from procedural complications as previously assumed[32]. Several cases of CTC-induced perforation have now been reported. These cases mostly have been associated with ulcerative colitis[33], Crohn's disease[34,35] or rectosigmoid obstruction[36], but occurrences in patients with normal colons have occurred as well[37,38]. Reviews in the United Kingdom and Israel have suggested that the rate of serious complications may be as high as 0.06%-0.08%[39,40], which approaches the complication rates reported for conventional colonoscopy. There also have been concerns about radiation exposure. The surface radiation dose received during CTC is approximately 0.44 rem, which is roughly equivalent to that of two abdominal radiographs[41]. Although this is a relatively small dose, multiple repeated scans at regular intervals for surveillance purposes can still lead to cumulative radiation doses that may be of concern[42]. Low radiation dose protocols have been investigated[43], but these do not appear to reduce overall radiation exposure in practice[44].

COST-EFFECTIVENESS

The cost-effectiveness of screening with CTC is uncertain. Several decision analysis computer simulation studies have tried to assess this question[45-48]. Sonnenberg has compared the cost-effectiveness of screening CTC and colonoscopy, and has found that to achieve cost-effectiveness similar to colonoscopy, CTC needs to have a compliance rate that is 15%-20% better than colonoscopy, or cost 54% less. Ladabaum's analysis has found that, if the sensitivities of the two tests are equal, conventional colonoscopy is more cost-effective than CTC unless CTC costs are 40% lower than those of colonoscopy[45]. The greater the prevalence of polyps in the screened population, the greater the cost advantage of conventional colonoscopy. A Canadian analysis has concluded that CTC marginally increases mortality, with projected deaths due to missed adenomas exceeding deaths prevented by avoiding perforation[46]. The most recent study has found that CTC would only be cost-effective if its cost is < 43% of the cost of colonoscopy[48]. However, the cost-effectiveness of CTC may be better if the analysis takes into consideration clinically useful extracolonic findings[49]. The use of computer-assisted detection may also improve cost-effectiveness[50]. Even though studies at expert centers have reported that only 7.9% of patients screened with CTC needed to be referred for colonoscopy[51], in routine clinical practice, the referral rate may be considerably higher (perhaps as high as 15%-20%). Therefore, further studies are needed to investigate this issue, preferably using real cost data in a cohort of prospectively followed patients.

FOLLOW-UP STRATEGIES

The proper approach to diminutive polyps (≤ 5 mm in size) seen on CTC, in which the risk of cancer is extremely low[52], is also unclear at this time. Referral of all patients with diminutive polyps for follow-up colonoscopy would dramatically increase the cost of CTC screening. The alternative approach, that is, following the polyp using repeat CTC at shorter intervals, would also be expensive and increase radiation exposure. Several decision analyses have simulated CTC screening with non-reporting of diminutive polyps and have reached conflicting conclusions regarding cost-effectiveness, outcomes and safety[53-56]. It has been estimated that up to 33% of screening patients with high-risk neoplastic lesions would be interpreted as normal if American College of Radiology guidelines on CTC reporting were followed (these guidelines recommend that polyps < 6 mm be ignored)[57,58]. This is because a significant fraction (almost 7%) of relatively small polyps may harbor advanced neoplastic tissue[59]. Furthermore, some surveys have indicated that most patients and physicians favor reporting of diminutive adenomas found during CTC[60]. It is also of concern that polyp size or location reported at CTC may not be accurate, when compared with pathological assessment or colonoscopic evaluation[61,62].

EXTRACOLONIC FINDINGS

Extracolonic abnormalities have been found during CTC in up to 50% of patients[63-65]. Although incidental detection of previously unsuspected pathology may benefit some patients, others will be subjected to needless anxiety and testing for what will ultimately turn out to be clinically insignificant lesions or false-positive results. Some studies have suggested that this may have significant cost implications[66,67], while others have not found this to be a problem[68,69].

CONCLUSION

At present, the exact clinical role of virtual colonoscopy

still awaits determination. Two types of patients for whom CTC is clearly useful are those with incomplete colonoscopy due to colonic tortuosity, and those with obstructive cancer that precludes passage of a colonoscope[70,71], although there is some concern that patients with incomplete colonoscopies might sometimes harbor occult perforation[37]. Currently, screening CTC is not covered by Medicare or any other public or private health insurance plan. The only exception is a limited program in Wisconsin; review of data from this program has shown similar detection rates of advanced neoplasia for colonoscopic screening *vs* CTC screening[51]. Even though widespread CTC screening is not available today, in the future there may eventually be a role for this technology. As a result of its general acceptance by patients, CTC offers the possibility of increasing the overall prevalence of colon cancer screening. One approach would be to offer CTC as the primary screening modality for all patients, followed by same-day colonoscopy if lesions are found[72]; alternatively, a risk-stratified strategy using colonoscopy for high-risk patients and CTC for low-risk patients might be more resource-efficient[73]. Currently, there appears to be enough multi-detector CT scanning capability in the United States to handle large-scale screening requirements, if needed[74,75]. Of course, a prerequisite for CTC screening programs is adequate training of all radiologists; gastroenterologists can also potentially be trained to read CTC results[76]. Although decision analyses have suggested that screening CTC can result in a decrease in colonoscopy volume[77], in practice, this has not been observed because the decrease in the number of primary screening colonoscopies is compensated for by an increase in colonoscopies for positive CTCs[78].

Technological advances in this area will undoubtedly continue, with multi-detector row CT scanners allowing thinner collimation and higher resolution images. Stool-tagging techniques are likely to evolve and may eventually allow for low-preparation or preparationless CTC. Perceptual and fatigue-related reading errors potentially can be minimized with the help of computer-aided detection software[79,80]. Further research will define the exact role of this promising technology in our diagnostic armamentarium.

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