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Computerized Tomographic Colonography versus Colonoscopy as a Screening and Diagnostic Test

Department: Nursing

Degree: Master of Science

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Computerized Tomographic Colonography versus Colonoscopy as a Screening and Diagnostic Test

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3-8-15

## PERMISSION

Title            Computerized Tomographic Colonography versus Colonoscopy as a Screening  
                  and Diagnostic Test

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### Abstract

Colorectal cancer remains a common cause of morbidity and mortality in both men and women. However, screening tests for colorectal cancer continue to improve the detection of polyps and cancer allowing for early intervention. Computerized tomographic colonography and colonoscopy are two tests available for the screening and diagnosis of colorectal cancer and cancer precursors. This review aims to determine if computerized tomographic colonography is as effective as colonoscopy as a screening and diagnostic test in the detection of colorectal cancer in patients over the age of 50. Overall, studies indicate that computerized tomographic colonography has similar sensitivity, both as a screening test and as a diagnostic test, for the detection of polyps and colorectal cancers. However, in patients where lesion size was  $< 10$  mm, sensitivity of computerized tomographic colonography decreases and colonoscopy screening proves more efficacious. Findings suggest that colonography can be used as a first-line screening and diagnostic test. Research also indicates that there is also a need to develop and implement evidence-based guidelines specific to the use of colonography, as well as for referral criteria once colonography has detected concerning lesions.

*Keywords:* colonoscopy, colonography, meta-analysis comparing CT colonography

## Computerized Tomographic Colonography versus Colonoscopy As a Screening and Diagnostic Test

Colorectal cancer screening remains one of the best cancer screenings available for patients today. Screening tests have greatly impacted the incidence, prevalence and death rates associated with colon cancer. Historically, colon cancer has ranked as one of the top two causes of cancer related deaths dating back to the 1940's (Siegel, DeSantis & Jemal, 2014). The most recent statistics indicate that colon cancer is now the third leading cause of cancer related deaths. Additionally, overall incidence rates have decreased by an average of 3.4% per year since 2001. "Declines since 1975 have been attributed to improvements in treatment (12%), changing patterns in colorectal cancer risk factors (35%), and screening uptake (53%)" (Siegel et al., 2014). Screening options are varied, allowing patients and providers to individualize a plan of care. According to the American Cancer Society's colorectal screening recommendations (2015), current imaging tests commonly used in the detection of polyps and colorectal cancer include flexible sigmoidoscopy (FS), colonoscopy, double-contrast barium enema (DCBE) and computerized tomographic colonography (CTC). Additionally, non-imaging tests used in the detection of colorectal cancer include guaiac fecal occult blood test (gFOBT), fecal immunochemical test (FIT), and stool DNA testing (sDNA).

Colonoscopy continues to be the "gold standard" for screening and diagnostic testing for colorectal cancer. It is currently the most used colorectal cancer screening in the United States (Allen, 2015). Benefits to using colonoscopy over other forms of diagnostic testing include the ability to visualize the entire colon, as well as the ability to remove polyps or take samples of tissue for biopsy if concerning lesions are identified. However, up to one fifth of lesions may not be detected with use of colonoscopy even though studies show that it has a high sensitivity and

specificity in the detection of colorectal cancer (Matsuda, Kawana & Chiu, 2015). Additionally, there are situations in which patients may not be suitable candidates for colonoscopy, i.e. patients who are debilitated, the elderly, patients at increased risk of sedation or those with underlying bleeding disorders (Pickhardt, 2010). These patients would benefit from a screening test that has proven to be as sensitive as colonoscopy in the detection of colorectal cancer, without additional risks.

Although CTC is a relatively new diagnostic tool for the detection of polyps and colon cancer, research continues to validate its use within the field of medicine. Multiple variables have been researched to determine its worth as a screening and diagnostic tool including patients' acceptance and preference for CTC versus colonoscopy, its cost-effectiveness in terms of outcomes in life-years saved, and its ability to accurately diagnose polyps and cancer in comparison to colonoscopy. Computerized tomographic colonography is similar to colonoscopy in that it requires bowel preparation and insufflation of gas into the colon for viewing just as colonoscopy does. However, it does not require the insertion of an endoscopic tube rectally for imaging. Imaging is completed through 2D or 3D radiological tomography. Patient preference for CTC as a screening test has been proven in multiple published studies supporting the idea that if patients are more comfortable with the test, they are more likely to get screened and ultimately diagnosed at an earlier stage (Lin et al., 2012; Howard et al., 2011). Nevertheless, it is important for providers to be aware of the sensitivity and specificity of a test in detecting what it is supposed to detect. The following review will address the screening and diagnostic value of CTC as compared to colonoscopy in both symptomatic and asymptomatic patients over the age of 50.

### Case Report

A 65 year old woman presented to the clinic with a six week history of constipation, blood in her stool and abdominal cramping. She was seeking care due to worsening of her symptoms, including increasing fatigue that was affecting her ability to do normal daily activities. The abdominal cramping she was experiencing occurred in the left lower quadrant of the abdomen. It typically lasted about 30 minutes and was worse within an hour of eating any food. She also complained of some discomfort in the right epigastric region that she rated 2/10 on the 0-10 pain scale. She had tried walking, resting and defecating to relieve the abdominal cramping without any improvement in her symptoms. She noticed bright red blood in her stool with bowel movements, and felt that this was partially due to being constipated as she was having to strain a lot with bowel movements and had stools that were smaller in diameter and amount. Subsequently, she had tried laxatives without any change in her stool consistency and only mild improvement in her abdominal symptoms. Additional symptoms that were of concern included night sweats, a decrease in appetite, and a 12 pound weight loss in the preceding four weeks. She denied having any nausea, vomiting, mucous in her stools or fevers. She denied having traveled outside the United States in the previous six months. Prior to her visit, she had never had a colonoscopy. Her family medical history was unknown to her, as she was adopted and she did not know any of her biological family.

Her medical and surgical history were unremarkable, and she did not have any allergies. Her medications consisted of a daily multivitamin. She was a nonsmoker and did not consume any alcoholic beverages. Her diet consisted of adequate amounts of fruits and vegetables and she drank about 3-4 cups of water each day. She typically exercised 3-4 times per week but had refrained from doing any physical activity since her symptoms began.

Her review of systems was negative except for the above mentioned constitutional and abdominal symptoms. The physical assessment revealed an ill-appearing, somewhat distressed woman. Vital signs were as follows: blood pressure 150/88, heart rate 72, respiratory rate 16 and a temperature of 97.3 F. Her head and neck exams were normal showing moist, pink mucous membranes and no evidence of glossitis or lymphadenopathy. Examination of her chest was unremarkable with clear, equal breath sounds bilaterally, no shortness of breath or chest pain, and normal heart tones, rate and rhythm. Abdominal exam revealed a tympanic abdomen with hypoactive bowel sounds, a 10 x 10 cm palpable mass in the left lower quadrant, and tenderness with palpation over the right upper quadrant with hepatomegaly appreciated. There were no aortic or iliac bruits detected with auscultation. Murphy sign, Rovsing sign, Cullen sign and Blumberg sign were all negative.

Testing for this patient included a complete blood count (CBC) and a guaiac fecal occult blood test. Results of the CBC showed the patient to have a microcytic, hypochromic anemia likely caused from the bleeding occurring within the gastrointestinal tract that was not only detected by the patient through direct visualization of blood in the stool, but was also shown through a positive guaiac fecal occult blood test. Interestingly, the patient underwent further testing of the colon with air contrast barium enema and flexible sigmoidoscopy instead of the "gold standard" colonoscopy. Results of the air contrast barium enema and flexible sigmoidoscopy showed the patient to have a 100% obstruction of the proximal colon due to an invasive and poorly differentiated adenocarcinoma. Subsequently, 20 pericolic lymph nodes were tested for cancer with four testing positive for metastatic tumor. Treatment for this patient included referral to oncology, and follow up was conducted per the recommendations of the oncologist and on an as needed basis.



When determining what type of screening or diagnostic test to utilize in patients who require further evaluation of their gastrointestinal symptoms, providers must consider multiple variables including contraindications to specific types of tests, patient preferences, and cost effectiveness of the intervention. Providers should also be aware of what tests are most sensitive and specific to the diagnosis of colorectal cancer in order to provide the patient with the best outcome possible. The following review will compare CTC and colonoscopy in their ability to detect polyps and colorectal cancers in patients over the age of 50.

## Literature Review

### Literature Search Strategies

Relevant published studies and journal articles relating to the use of CT colonography in comparison to colonoscopy were obtained from the electronic databases CINAHL, PubMed and Cochrane Library. References were retrieved through CINAHL using keywords that included *colonography* and *colonoscopy* with the Boolean operator *AND*. Additional filters were added to this search, including publication date of 2009-2014 and in the English language. This yielded 78 results, of which two meta-analyses were obtained and utilized. PubMed was used with the keywords *meta-analysis comparing CT colonography* yielding 7 results. Four of these results were further reviewed and used for supporting information. Under the *related citations* there were an additional 1289 articles. Once the filters for publication date of five years, English language, human species and full text articles were applied, there were 271 articles for review. All article titles were reviewed. This yielded one meta-analyses, two random-control trials, two retrospective studies and one observational study. Cochrane Library was additionally searched for relevant articles, however there were no additional studies found. Reference lists of the

obtained articles were also reviewed, as well as current published colorectal screening guidelines.

### **Summary of Findings**

In a systematic review and meta-analysis conducted by Pickhardt, Hassan, Halligan and Marmo (2011), researchers evaluated studies that were conducted to determine the accuracy of CTC detection of colorectal cancer in comparison to colonoscopy in both symptomatic and asymptomatic patients over the age of 50. Results of this review show that CTC sensitivity in the detection of colorectal cancer overall was 96%, while colonoscopy had a sensitivity of 95% (Pickhardt et al., 2011). Researchers found that in cases where a cathartic bowel preparation and faecal tagging were used, CTC did not miss any cancers (Pickhardt et al., 2011). CTC may also prove to be better than colonoscopy in the evaluation of right-sided colorectal cancers where passing of the endoscope becomes more difficult and where most missed cancers are found with the use of colonoscopy screening (Pickhardt et al., 2011).

These results were duplicated in a multicentre randomized trial conducted by Atkin et al. (2013) where patients aged 55 years or older were referred for colonoscopy due to symptoms suggestive of colorectal cancer with the most frequent symptoms being a change in bowel habit, rectal bleeding or abdominal pain. Patients were randomly assigned to receive either colonoscopy or CTC with the primary outcome measure being the proportion of patients who required additional colonoscopic investigation for concerning lesions. Secondary outcome measures included colorectal cancer detection and miss rates, extra-colonic cancer diagnosis with the use of CTC, and serious adverse events. Researchers found that “the overall detection rate of colorectal cancer or large polyps did not differ between groups” with 11.1% of patients diagnosed who underwent colonoscopy and 10.7% of patients diagnosed who underwent CTC

(Atkin et al., 2013, p. 1198). This resulted in 5.6% of CTC patients and 5.7% of colonoscopy patients receiving a definitive colorectal cancer diagnosis, ultimately resulting in similar sensitivity (Atkin et al., 2013). Additional findings included factors that may affect a provider's decision to utilize CTC. For example, researchers found that extra-colonic malignancies were found in 9 of 48 patients referred for additional investigation based on CTC findings (Atkin et al., 2013). They also found that 30% of patients who underwent CTC required further testing with colonoscopy due to uncertainty of smaller polyps, and/or the diagnosis at the end of the screening test was unclear resulting in higher false-positives. This resulted in patients receiving additional diagnostic testing three times as often as those who underwent colonoscopy. With colonoscopy only 8% of patients required additional colonic investigation (Atkin et al., 2013). Kim, Pickhardt, Hanson & Hinshaw (2010) found that referral rates increased in older patients who underwent CTC and required further investigation of colonic lesions. Nonetheless, the overall referral rate was similar to those of other screening tests in similar age groups. These statistics when put into terms of medical practice, ultimately start affecting patient experience, providers' time, and cost-effectiveness of the screening test.

Stoop et al. (2012) also conducted a randomized control study on asymptomatic patients over the age of 50 looking at the primary outcomes of patient participation rates in screening, as well as diagnostic value between CTC and colonoscopy. The findings of their study show that although CTC and colonoscopy are similar in detection rates of advanced neoplasia, colonoscopy proved to be more efficacious, where 6.1% of participants were diagnosed with the use of CTC and 8.7% of participants were diagnosed with the use of colonoscopy. An additional meta-analysis published by de Haan, van Gelder, Graser, Bipat & Stoker (2011) looked at polyp and cancer detection through use of CTC in asymptomatic patients as well. They concluded that CTC

has a higher sensitivity for adenomas more than 10 mm in size in comparison to colonoscopy. However, the sensitivity of CTC decreased as the size of the adenoma decreased, indicating that it may be limiting in the detection of smaller polyps and neoplasias. Researchers also found that the sensitivities obtained within their study were lower than the estimated sensitivities for polyp detection in some of the previously published studies. However, calculation of estimated sensitivity and specificity was done using statistical analyses “in which the individual studies are weighted by number of included participants” (de Hann et al., 2011, p. 1756.). An additional meta-analysis conducted by Rosman & Korsten (2005), showed similar results to de Haan, et al. (2011) where CTC sensitivity and specificity was sufficient in detecting large polyps. However, colonoscopy had statistically significant higher sensitivities and specificities for detecting smaller polyps.

Kim, Pickhardt, Hanson & Hinshaw (2010) used an observational study design to look at the use of CTC versus colonoscopy in patients 65-79 years old. Less invasive screening tests or comorbid conditions that may increase adverse events with the use of colonoscopy may be reasons that patients in this age cohort would find CTC more suitable. Findings show that although researchers were unable to determine exact sensitivity and specificity of CTC in comparison to colonoscopy due to the observational design of the study, prevalence of colorectal cancer determined through use of CTC was similar to that described in other studies with a 7.6% prevalence rate of advanced neoplasia. These results are slightly higher than that reported in the study by Atkin et al. (2013). However, the overall increase in prevalence could be expected with the increased occurrence that typically increases with age. Kim et al. (2010) also found overall CTC-colonoscopy concordance rates to be similar between different age groups. The National CT Colonography Trial (Johnson, 2012) duplicated these results in a study comparing CTC

sensitivity and specificity in two different age cohorts. Results show that between the two age groups there is no statistically significant difference in the sensitivity and specificity of detecting lesions larger than 10mm, or for neoplasias 6-9 mm in size (Johnson, 2012).

Research has also proved CTC to be highly sensitive in the diagnosis of additional cancers found proximal to a stenosing colorectal cancer as well as in the localization of tumors (Park et al, 2012). However, in comparison researchers also found CTC to be less sensitive in the detection of non-cancerous lesions in those with an underlying stenosing colorectal cancer (Park et al., 2012).

Current colorectal screening guidelines through the American Cancer Society (2015), the American College of Radiology (2014), the US Multi Society Task Force on Colorectal Cancer and the American College of Gastroenterology (Rex, Johnson, Anderson, Schoenfield, Burke & Inadomi, 2009) support the use of CTC as a screening and diagnostic test for patients over the age of 50. The American College of Gastroenterology colorectal screening guidelines actually suggest the use of CTC in place of DCBE due to its higher sensitivity and specificity for detecting colorectal polyps (Rex et al., 2009; Sosna et al., 2008; Halligan et al., 2013). All of these guidelines found similar strengths and limitations to the use of CTC as a screening and diagnostic test. Strengths of using CTC include similar sensitivity and specificity for the detection of large adenomas as compared to colonoscopy, lower risk of adverse events due to the test being less invasive than colonoscopy, and detection of extra-colonic findings (Levin et al., 2008). One of the limitations of CTC use mentioned within the guidelines includes the use of radiation for imaging. "The additional lifetime risk of cancer in any site associated with a single CTC examination at age 50 years was 0.14%" (Levin et al., 2008). However, with established low dose parameters, risk can likely be reduced although long-term effects are still unknown.

Other limitations cited within the guidelines include the lack of standardized reporting and management of abnormal lesions found on CTC, which ultimately affects the efficacy and usefulness of the test. The United States Preventative Services Task Force (USPSTF) guideline on colorectal cancer previously found insufficient evidence in support of using CTC as a screening test for colorectal cancer. However, this guideline is currently under revision and will likely include a stance on its use in light of current literature findings (USPSTF, 2014).

Multiple research studies have been conducted on the accuracy and diagnostic value of CTC in comparison to colonoscopy. However, studies overall display significant heterogeneity with variations in how the screenings were conducted, the experience of the radiologist interpreting the screenings, whether patients were symptomatic or asymptomatic and what the primary outcomes were. Colonoscopy is often used as the reference standard for both tests, which additionally could lead to underestimating or overestimating the sensitivity of either test. It is recommended that further testing on the diagnostic value of CTC continue with the intention of developing more comprehensive patient management guidelines.

### **Learning Points**

According to the results of the literature review comparing CTC to colonoscopy as a screening and diagnostic test, the following key points and supporting evidence are provided:

- CTC sensitivity is comparable to colonoscopy sensitivity for detecting colorectal cancer and lesions  $\geq 10$ mm. It is less accurate than endoscopic colonoscopy for detecting smaller polyps (Pickhardt, Hassan, Halligan & Marmo, 2011; de Haan, Pickhardt & Stoker, 2015; Rosman & Korsman, 2005).
- CTC can be used as an additional first-line screening and diagnostic test for the detection of polyps and colon cancer in patients who are unable to undergo colonoscopy or who

prefer CTC (de Haan, Pickhardt & Stoker, 2015; Pickhardt, Hassan, Halligan & Marmo, 2011; Atkin et al., 2013; de Haan, van Gelder, Graser, Bipat & Stoker, 2011; Park et al., 2012).

- Evidence-based guidelines need to be developed in order to establish a framework for providers to use CTC in the most effective way and assist providers in determining when to refer patients for further colonoscopy (Atkin et al., 2013; de Haan, Pickhardt & Stoker, 2015). With the higher occurrence of additional colonic testing required with CTC, it would be valuable for patients to receive colonoscopy following CTC being they have already completed the bowel prep required for both. Workflow of patients who require additional testing should be included in the guideline. Additionally, the size of polyps that require referral for further testing should also be included in the guideline, as research has shown that sensitivity of CTC decreases as the size of the polyp or lesion increases (Atkin et al., 2013; de Haan, Pickhardt & Stoker, 2015). “At present, no clear polyp-size threshold for referral has been identified based on the available sensitivity and specificity reports” (Parekh, Rouzbeh, Oldfield, Nicholas & Johnson, 2014, p.745).
- Further research needs to be conducted on how CTC affects colon cancer prevalence and death rates long-term, as well as its ability to impact financial healthcare costs both short-term and long-term. Establishing this data would provide continuing support for or against the use of CTC as a screening and diagnostic test, as well as help in determining the cost-benefit ratio and potentially reimbursement through health insurance carriers such as Medicare. Currently, Medicare does not cover CTC screening for colorectal cancer (Centers for Medicare and Medicaid Services, 2009). However, their last systematic review of literature was conducted in 2008 before much of the recent literature

was published supporting the diagnostic value of CTC. Many factors have been found to influence the cost-effectiveness of CTC including patient adherence and compliance rates, natural history of the disease, extra-colonic findings, management of polyps and lesions found on CTC, and sensitivity of the test (Kriza et al, 2013). The variation in these factors provide reason to support the continued research on CTC as a screening and diagnostic test.



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