CT colonography : can it be used as a primary screening method for colorectal cancer in place of standard colonoscopy?

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Dedication

I would like to dedicate this project to Ryan, to my family, and to all of my friends. Without your encouragement and support to follow my dream, I would not have been able to make it this far! You all mean the world to me!

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I would like to acknowledge and thank my project advisor, April Gardner, for all of her help and guidance throughout this project. Thank you for helping to take this project from tedious research to a fantastic learning experience!

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Introduction

Colorectal cancer (CRC) has a significant impact on the lives of many people in this country every year. Colorectal cancer is the third most commonly diagnosed cancer in both men and women and is the third leading cause of cancer death (Jemal, et al., 2008). It is estimated that 148,810 men and women will be diagnosed with CRC and 49,960 will die from it this year. Based on CRC trends from 2003 to 2005, 1 in 19 men and women will be diagnosed with CRC during their lifetime (Ries, et al., 2007). Due to the significance of this problem, there has been much focus on reducing the mortality from this disease. A goal set by Healthy People 2010 hopes to decrease mortality of CRC from 21.2 per 100,000 people in 1998 to 13.9 per 100,000 (U. S. Department of Health and Human Services, 2000, November). Prevention and early identification through screening for colorectal cancer is currently the most successful method of achieving this goal.

The primary care setting is the most common place patients receive information on CRC screening. A study of patient-provider communication on patient use of CRC screening methods reported that communication played a vital role in a patient's decision to get screened (Carcaise-Edinboro & Bradley, 2008). These authors found patients who identified receiving adequate time and explanation about CRC screening from their primary care provider were more than two times more likely to obtain screening than those who did not. This identifies a great opportunity for physician assistants in primary care to improve CRC screening rates.

Physician assistants have continued to gain increasing autonomy in the primary care setting and are often the primary providers for many patients in their practice. Patient education is one area that physician assistants continue to make an increasingly important impact. A study by Shaheen and colleagues (2000) on primary care nurse practitioner and physician assistants'

practices and attitudes of CRC screening identified that these practitioners continue to play an increasingly cost-effective role in providing CRC screening. Despite this, one in five practitioners in this study identified a lack of knowledge about CRC screening recommendations as a significant barrier to providing this information to patients. This suggests that a review of CRC and its screening recommendations and methods would improve physician assistants' abilities to provide adequate and appropriate information about it to their patients.

It is a goal of this paper to provide physician assistants with a review of CRC and CRC screening recommendations. This article also specifically addresses one type of test for colorectal cancer that has recently gained more widespread acceptance. Computed tomographic (CT) colonography, also known as virtual colonoscopy, is a radiologic test that allows for viewing the colon to detect for pre-cancerous and cancerous lesions. It is important that physician assistants are knowledgeable of this test to be sure they are providing patients with both accurate and complete information on CRC screening.

Literature Review

Pathophysiology of CRC

The pathophysiology of CRC has been both well studied and understood. Most CRC develops from adenomatous polyps that become hyperproliferative and dysplastic. The change from adenoma to cancer occurs as a multi-step process known as the adenoma-carcinoma sequence (Muto, Bussey, & Morson, 1975). In the normal colon, surface cells undergo exfoliation and apoptosis and are continuously replaced by new epithelial cells that undergo proliferation at the crypt. The proliferation to form new cells normally ceases as the cells leave the crypt and get near the mucosal surface. At the surface, the cells terminally differentiate into normal mucosal epithelium.

Adenomas occur when the normal epithelial cell proliferation and differentiation becomes disrupted. New epithelial cells undergo genetic mutations and enter a state of hyperproliferation and dysplasia. The cells fail to stop proliferating at the crypt, and abnormal proliferation leads to an adenoma. The adenoma-carcinoma sequence is supported by observations that early carcinomas usually occur within an adenomatous polyp and adenomas are usually present 10 to 15 years prior to cancer in both sporadic and familial cases (Muto, et al., 1975). The slow growth of an adenoma to cancer allows for a unique opportunity to catch the potentially deadly adenoma before this change occurs.

Adenomatous polyps make up about two-thirds of all colon polyps; however, their progress to cancer depends on multiple and cumulative factors. Not all adenomas develop into cancer. Both genetic and environmental factors influence the likelihood of developing CRC from an adenoma. Vogelstein and colleagues (1988) suggest multiple genetic mutations are required for malignant transformation of the adenoma to cancer. It is the multi-step

accumulation of genetic mutations that leads to high-grade dysplastic changes in an adenoma and progression to malignancy.

Two common types of mutations are germline and somatic mutations. Germline mutations occur within the sperm or egg and can be passed to offspring. Specific germline mutations can lead to an inherited predisposition to developing CRC, such as those with family adenomatous polyposis. Individuals with these mutations, as well as those with a personal or family history of CRC without genetic predisposition, and those with inflammatory bowel disease, make up approximately 25% of all CRC (S. J. Winawer, 1999). Individuals in these groups are considered to be at high risk of developing CRC and are strictly and regularly monitored.

Somatic mutations occur sporadically in body cells during growth and differentiation of cells in a tissue. Somatic mutations are responsible for most sporadic cases of CRC (Muto et al., 1975). Sporadic disease, or CRC occurring in average risk patients, is the largest group of CRC, accounting for approximately 80% of all cases (Ferrucci, 2006). Individuals with an average risk of developing CRC include those age 50 years and over who do not demonstrate inherited or other risk factors. On average, it takes ten to fifteen years for a small adenoma to acquire the genetic changes necessary to develop into cancer (Muto, et al.).

Adenomas at considerable risk of progressing to CRC are those with high grade dysplasia. The most significant clinical factors identified in the progression of an adenoma to CRC, in addition to the presence of high grade dysplasia, are the size and histology of the polyp. The National Polyp Study found the percentage of adenomas containing high-grade dysplasia increased with both increasing size and villous histology of the adenoma (O'Brien, et al., 1990). Support for these findings was demonstrated in another study of colon polyps that found

adenomas of increasing size and villous histology were associated with higher rates of severe dysplasia and malignancy (Aldridge & Simson, 2001). Adenomas 10 mm and greater were found to be the most at risk for high grade dysplasia. The term advanced adenoma is applied to those adenomas greater than ten millimeters, having high grade dysplasia, or having villous histology, and these are the most clinically significant adenomas (Levin, et al., 2008) .

Adenomas less than ten millimeters have demonstrated a much lower risk of progression to cancer. Small adenomatous polyps, or polyps 6 to 9 mm in size, are most commonly benign. Over 90% of these polyps do not contain high grade dysplasia, and less than 1-2% of polyps in this range contain invasive cancer (Aldridge & Simson, 2001; Shinya & Wolff, 1979). The risk of cancer associated with small polyps increases when these polyps contain a villous component or when there are multiple small polyps present (O'Brien, et al., 1990). It is widely accepted that polyps 5 mm and smaller, known as diminutive polyps, are most commonly hyperplastic with less than 1% risk of growth into CRC (Shinya & Wolff). Polyps less than 5 mm have been determined to be clinically insignificant.

Age has been found to be one of the most significant risk factors for cancer development in average risk persons. The National Polyp Study found the incidence of adenoma development to be highest in those over the age of fifty years, and the incidence increased with each decade of life (O'Brien, et al., 1990). Ninety percent of all cases of CRC in average risk individuals arise in those fifty years of age and older (Ries, et al., 2007). Both the National Polyp Study (O'Brien, et al.) and the study by Aldridge & Simson (2001) also found the majority of high grade dysplastic adenomas arose primarily in the left colon after the splenic flexure; however, recent trends have shown an increase in CRC in the ascending colon (Nelson, Dollear, Freels, & Persky, 1997; Obrand & Gordon, 1998; Troisi, Freedman, & Devesa, 1999).

Environmental factors also play a role in the risk of CRC. The American Cancer Society identifies lifestyle factors such as smoking, obesity, physical inactivity, alcohol consumption, and diets high in red meat as potentially increasing the risk of developing CRC. The association between diet, exercise, and weight with CRC are stronger than for most other cancers (American Cancer Society, 2008, March). Managing these risk factors through lifestyle modification can help to reduce the risk of CRC.

CRC Screening

Currently, the best method for protecting against CRC in average risk, asymptomatic adults is early detection and removal of adenomatous polyps. Removal of adenomatous polyps interrupts the adenoma-carcinoma sequence, thereby preventing its progression to CRC (Grinnell & Lane, 1958; Muto, et al., 1975; S. J. Winawer, et al., 1993). The rates of mortality from CRC have been trending downward since the mid-1980s (Ries, et al., 2007), and it is believed to be the result of an increase in screening for CRC (Pignone, Rich, Teutsch, Berg, & Lohr, 2002). Current screening methods aimed at detecting cancer and adenomatous polyps allow for early treatment to prevent invasive cancer.

Despite the evidence supporting early regular screening, there is a large deficiency of recommended use of colorectal screening methods by today's society. One report suggests approximately 40% of the population of the United States does not get regular colorectal screening ("Use of colorectal cancer tests," 2008). Seeff and colleagues (2004) found 41.8 million average risk people age fifty and over in the United States were not being appropriately screened for CRC. Although screening for CRC has been shown to be effective in reducing the mortality from this disease, these studies show a large number of this country's population in need of CRC screening is not getting it.

CRC Screening Recommendations

CRC screening recommendations have been offered by various organizations over the past thirty years in attempts to increase the use of screening methods for early detection. These recommendations serve as research supported guidelines for appropriate testing methods and time intervals to screen for CRC and continue to be updated as new research and screening methods prove effective. Initial recommendations for CRC were issued by the American Cancer Society in 1980 (Eddy, 1980). Additional recommendations were made by the U.S. Preventative Services Task Force in 1996 and were later reorganized in 2002. This organization recently issued an updated statement of recommendations in 2008 (U.S. Preventive Services Task Force).

In March of 2008, the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology joined to issue guidelines for screening for CRC in average risk adults (Levin, et al., 2008). These organizations collaborated to systematically review available evidence-based research and expert opinion on CRC screening methods. The guidelines provide a modern multi-organizational consensus on acceptable screening recommendations for the average risk population age 50 years and over. These organizations have identified a goal of providing the best recommendations to allow for early detection of CRC and reducing mortality from advanced colorectal disease (Levin, et al.).

The recommendations established by the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology divide currently accepted screening methods into two categories: those that primarily test for CRC (Table 1) and those that detect both adenomatous polyps and cancer (Table 2). It is their recommendation that tests in the latter category should predominantly be encouraged as evidence has shown they are more successful in early identification and prevention of CRC, which can

improve disease survival rates (Levin, et al., 2008). It is recommended that screening in the average risk population begin at age 50 years and continue every five to 10 years throughout the remainder of life.

Guaiac-based fecal occult blood test (gFOBT), fecal immunochemical test (FIT), and stool DNA test (sDNA) are tests used for the detection of CRC. The advantages of these tests are they are simple, noninvasive, and can be done at home. Despite this, these tests have many disadvantages and limitations. These tests detect the presence of cancer rather than prevent it, they must be done correctly and regularly to be effective, and positive abnormalities on any of these tests will require more invasive testing (Levin et al., 2008). Because these tests fail to detect adenomatous polyps, screening methods that offer a view of the colon to detect adenomatous polyps and prevent cancer are strongly encouraged.

Flexible sigmoidoscopy, colonoscopy, double contrast barium enema, and computed tomography (CT) colonography are currently the only tests available that offer a structural view of the colon. A structural view provides the ability to detect the presence of adenomatous polyps as well as cancer. Colonoscopy, double contrast barium enema, and CT colonography allow for the examination of the colon and rectum in its entirety. Examination of the entire colon is adventitious because of the importance of viewing the proximal colon. In addition to a growing trend in proximal adenomas mentioned earlier, Imperiale and colleagues (2000) found the presence of adenomatous polyps in the distal colon of average risk individuals age 50 years and over increased the risk of advanced adenomas in the proximal colon.

Flexible sigmoidoscopy is limited to examination of the rectum, sigmoid colon, and, in certain instances, the descending colon. This method is not able to detect adenomas in the proximal colon. Use of double contrast barium enema imaging technique has been declining in

recent years in the United States due to its labor intensiveness, low reimbursement rates, and lack of professionals to perform it (Levin, et al., 2008). Colonoscopy is currently accepted as the "gold standard" for colorectal cancer screening as it also allows for polypectomy, or removal, of lesions found on exam of the complete colon.

Of the structural exams recommended, CT colongraphy is the newest recommended screening method. CT colonography, first described in the mid-1990s, was not incorporated into past recommendations for CRC screening due to a lack of evidence to support its use. New advancements and evidence supporting effectiveness of CT colonography in the detection of adenomatous polyps and CRC has led the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology to include it in their 2008 recommendations (Levin, et al., 2008). They suggest screening for CRC using CT colonography every five years after the age of 50. Not all organizations agree with the use of CT colongraphy. In their 2008 updated statement of previous recommendations, the U.S. Preventive Services Task Force concluded there is insufficient evidence related to the balance of benefits to harm to recommend this test as a method of screening. Conflicting views on the use of CT colongraphy have contributed to limitation of its use for screening for CRC in the past.

CT colonography

CT colonography is a minimally invasive technique for examining the entire colon and rectum. First introduced in 1994, CT colonography has evolved due to technological advances in CT scanners and computer imaging. These advances have brought about an increased medical and scientific interest into the possibilities for its use.

With CT colonography use, images of the colon and rectum are obtained using a CT scanner. This differs from standard optical colonoscopy in there is no instrument inserted within

the rectum and colon for imaging. With the development and use of the multi-detector CT scanner, images taken in CT colonography have significantly improved by taking thinner slices in less time and with a single breath hold (O'Hare & Fenlon, 2006). Scanning of the patient occurs in both supine and prone positions to allow for alternative views if one position produces poor images. Yee and colleagues (2003) examined the use of supine and prone positions for polyp detection in patients and found a significant improvement in the sensitivity of detection of polyps of any size in most areas of the colon using both views in combination as compared to alone. They concluded that each view demonstrated better distention in specific areas of the colon, and therefore both views together offered superior visualization of polyps in all areas of the colon.

The images obtained from the CT scanner are then transferred to a radiological reading station containing special viewing software. The images are interpreted by a radiologist using two dimensional and three dimensional views. The two dimensional view allows for a standard CT view of the colon, while the three dimensional view offers a virtual reconstruction of the inside of the colon. An early study by Hara, Johnson, Reed, Ehman, & Ilstrup (1996) comparing the two views found that using both views together resulted in better detection of polyps. Another more recent study by Pickhardt, Lee, and colleagues (2007) comparing both views suggested that three dimensional views greatly improve polyp detection by enhancing polyps located around colonic haustral folds that may appear similar to each other on the two dimensional view. The ability to see around haustral folds may be an advantage of CT colonography as most lesions missed by standard colonoscopy occur behind these folds (Pickhardt, Nugent, Mysliwiec, Choi, & Schindler, 2004). The use of multiple views of the

colon and rectum offers a unique method of detecting adenomatous polyps and cancer that may be otherwise missed.

Review of the images by a radiologist generally takes a short time and patients receive their results within a few hours. The protocol followed after adenomatous polyp detection has been the subject of much debate. Current recommendations by the American College of Radiology CT Colonography Practice Guidelines state those lesions 10 mm and over should be identified and described, while those with lesions less than 5 mm should not be reported. Lesions 6 to 9 mm should be reported when they are identified with reasonable probabilities (American College of Radiology, 2006).

A model protocol CT colonography screening currently used by the University of Wisconsin CT Colonography Screening Program identifies specific actions to be taken when adenomatous polyps are identified (Kim, Pickhardt, Hoff, & Kay, 2007). This model serves as the standard protocol guide for CT colonography screening (Table 3). Patients identified with adenomatous polyps 10 mm or greater in size or greater than two 6 to 9 mm polyps should receive immediate referral to colonoscopy for polypectomy. If two or less polyps 6 to 9 mm are identified, patients may individually choose to have them removed or undergo a strict monitoring schedule. This schedule includes screening with CT colonography every year for those polyps 8 or 9 mm or every two years for polyps 6 to 7 mm. No action is taken for polyps 5 mm or less. The inability of CT colonography to remove significant lesions is a disadvantage of this type of screening method as patients with large polyps must then undergo the additional procedure of colonoscopy to have them removed.

Accuracy of the CT colonography depends on appropriate patient preparation. Fluid and stool within the colon can hide adenomas and cancer, therefore causing these important lesions

to be missed (Yee, 2006). Large amounts of stool could be misinterpreted as an adenoma and cause unnecessary alarm for both the patient and the physician. In order to prevent these situations from occurring, vigorous bowel cleansing, similar to that used in standard colonoscopy, is used to remove fluid and stool from the colon and rectum (Yee). The method of bowel cleansing established by the American College of Radiology CT Colonography Practice Guidelines involves the rigorous use of dietary restriction, hydration, osmotic laxatives, and contact laxatives in combination (American College of Radiology, 2006). Patients commonly follow a high fiber diet for a few days prior to the study, and laxatives are administered the day prior to the examination for complete emptying of the colon. This method requires significant active compliance from the patient and may interrupt their normal daily activity.

The vigorous bowel cleansing required by CT colonography has led to patient reluctance to using this technique. Recently, methods of stool and fluid tagging have been investigated to reduce or eliminate the need for bowel cleansing. Stool and fluid tagging involves the ingestion of contrast material, such as barium or iodine, 24 to 48 hours prior to CT colonography (Lefere & Gryspeerdt, 2006). The contrast mixes with fluid and stool to appear white, allowing the radiologist to differentiate it from soft tissue density of a polyp on the two dimensional view (Lefere & Gryspeerdt). Only minimal bowel cleansing is used with this method, thereby reducing patient burden. While recent studies have demonstrated support for using this method (Lefere, Gryspeerdt, Marrannes, Baekelandt, & Van Holsbeeck, 2005), the American College of Radiology Practice Guidelines for the Performance of CT Colonography currently does not support its use due to “limited validation in clinical trials” (American College of Radiology, 2006).

In addition to bowel cleansing, accuracy of CT colonography also depends on adequate distention of the colon. A colon that is not properly distended can limit polyp or cancer detection or could cause narrowing of the colon that can be misinterpreted as cancer (Yee, 2006). Colon distention is achieved by the insuffulation of gas into the colon through a tube that is inserted into the rectum. Patients may experience pain or discomfort as a result of this. Antispasmodic agents can be used to help relieve discomfort or for colon spasm if necessary (American College of Radiology, 2006). Anticholinergic side effects, however, are often common with their use.

Oxygen is the most commonly used gas in colon distention, but the use of carbon dioxide has increased recently as it has been shown to decrease patient discomfort. Shinners and colleagues (2006) found patients reported decreased discomfort after the procedure with carbon dioxide use. They also concluded that carbon dioxide improved distention of the transverse, descending, and sigmoid colon. Carbon dioxide is quickly absorbed by the bowel and exhaled by the lungs, thereby decreasing time of post procedure discomfort. Despite this, oxygen is still most commonly used due to cost and availability. Once insuffulation is complete, the CT scan is performed in supine and prone positions. Additional insuffulation may be required between positions for accurate imaging.

CT colonography has many procedural advantages over standard colonoscopy. It is less invasive; therefore, risks associated with presenting a medical device through the colon are reduced. The most common complication associated with CT colonography is perforation of the rectum or colon due to insuffulation of gas. In a multi-institutional study of 11,870 patients receiving CT colonography, the perforation rate was 0.059% or 1 in 1696 patients (Sosna, et al., 2006). The risk of perforation in this procedure is low and is less than seen with standard colonoscopy. In addition, CT colonography does not require sedation and takes less time to

complete than standard colonoscopy. Recovery time is quicker, and patients do not require assistance to drive home. Patients are also not required to discontinue medications, such as anticoagulants, prior to the procedure as they are in standard colonoscopy. Due to its limited invasiveness, CT colonography has less procedural related requirements from the patient on the day of its completion.

Despite these advantages, CT colonography is not without its flaws. CT colonography involves patient exposure to specific amounts of radiation. Using low dose techniques to minimize radiation exposure is standard for this procedure. Patient exposure using the low dose method has been estimated to range between 35-75 mA for supine and prone each, but the lifetime risk of cancer as a result of this exposure is estimated to be 0.14% for a 50 year old and half that for those 70 years and older (Brenner & Georgsson, 2005). Due to its limited time in use, there are no definite long-term statistics on the occurrence of cancer as a result of this procedure. The American College of Radiology (2006) encourages those performing this procedure to minimize radiation doses within the level of maintaining quality of the results.

Another disadvantage of CT colonography is the requirement of specialized training to accurately interpret its results. The ability to accurately interpret the data from the images greatly influences use of CT colonography as a valid method of CRC prevention. In a study comparing CT colonography trained radiologists to untrained radiologists, untrained radiologists demonstrated significantly poorer identification of polyps on CT colonography results (Slater, et al., 2006). The accuracy for identifying polyps 6-9 mm and 10 mm or greater was 64% and 100% respectively for radiologists trained to read CT colonography. Accuracy among untrained radiologists in identifying the same lesions ranged from 16.7-41.7% for 6-9 mm polyps and 16.7-83.3% for polyps 10 mm and greater. This suggests that a lack of training can reduce the

accuracy for identifying significant lesions and supports the need for training and experience in reading CT colonography images to improve its accuracy. The need for radiologists to gain specialized training and experience in CT colonography in order to improve the accuracy of interpreting CT colonography places a limitation on its implementation in all medical settings.

The utilization of CT colonography in screening for CRC has been greatly influenced by financial reimbursement for the procedure. Currently, CT colonography as a screening method in asymptomatic individuals is not covered by Medicare or most private insurance companies (Knechtges, et al., 2007). Coverage for this procedure by most insurance is limited to symptomatic patients in instances in which standard colonoscopy is unsuccessful or unable to be performed. Incomplete colonoscopy occurs when there is failure to reach the cecum with the endoscope, and occurs in approximately 8 to 35 percent of attempted colonoscopies (Odulate & Doenraad, 2006). Spasm, diverticulitis, strictures, adhesions from a previous surgery, or the presence of an obstructing cancerous lesion can prevent the scope from advancing through the proximal colon. CT colonography is often used in these cases.

CT colonography is also reimbursed by most insurance companies for use in those individuals in whom colonoscopy is contraindicated (Knechtges, et al., 2007). Contraindications include those with bleeding disorders, those unable to discontinue their anticoagulants, those unable to undergo sedation, or those with adverse events in prior colonoscopy. In addition, CT colonography is often approved for pre-operative evaluation of cancer wall invasion and staging (Knechtges, et al.). Current insurance coverage of CT colonography varies depending on the insurance company and the clinical situation; however, limited coverage as a screening method has restricted its widespread use.

The increased recognition of CT colonography as a potential valuable CRC screening method has led to strides to improve reimbursement for this procedure. CT colonography has recently gained assignment of two category III CPT codes, 0066T for screening CT colonography and 0067T for diagnostic CT colonography, from the American Medical Association (Knechtges, et al., 2007). Current Procedural Terminology (CPT) codes are the method by which medical services are documented and reimbursed. Category III codes are used for gathering data and tracking use of emerging medical services (Knechtges, et al.). Information gathered is then analyzed for development of CPT I codes, and these codes are commonly accepted for coverage by Medicare and private insurance (Knechtges, et al.). While not currently covered by Medicare, the granting of a Category III CPT code is an important step toward gaining insurance coverage for widespread use of CT colonography as a screening tool for CRC.

Contraindications to the use of CT colonography are very few. Absolute contraindications are associated with problems relating to the abdomen, including acute abdomen, acute diverticulitis, or recent surgery, that make insuffulation of the colon dangerous (Odulate & Doenraad, 2006). In addition, they identify contraindications unique to this procedure as weight restrictions of the CT scanner and possible patient claustrophobia. CT colonography is not recommended for those who are pregnant due to potential fetus exposure to radiation or for those with metal hip prostheses. The metal from a hip prosthesis causes artifact on CT images and makes it difficult to visualize areas of the colon around it (Odulate & Doenraad). Overall, CT colonography has been shown to be a versatile screening method that can be used in a majority of the population.

Future Developments in CT Colonography

CT colonography continues to evolve as new equipment and techniques are investigated and new discussions involving its use arise. Research investigating CT colonography without the use of cathartic preparation is an area of increasing focus. This type of procedure involves the ingestion of barium or iodine for fecal tagging on the day of the exam without the diet restrictions or laxative use normally required prior to the exam. Fecal tagging and electronic cleansing of the colon, or digital bowel cleansing, subtracts fluid and stool and allows for better reading of the colon (Summerton, Little, & Cappell, 2008). Because bowel preparation has been found to be a limiting factor in CRC screening test use, this reduced bowel preparation may improve patient participation in screening (Edwards, et al., 2004; Juchems, Ehmann, Brambs, & Aschoff, 2005; Scott, et al., 2004; Thomeer, et al., 2002). Reduced cathartic preparations are currently only being investigated for use in CT colonography; however, preliminary studies show promising results (Iannaccone, et al., 2004).

Computer-aided detection has also become a major area of investigation for use in CT colonography. Computer-aided detection is a computer program that provides automated detection of polyps and masses in the colon (Yoshida, 2006). The program marks potentially suspicious polyps on the 2D and 3D images and allows the radiologist to further investigate the area in question. It is designed to improve accuracy when reading the CT images, but it will not replace a complete and thorough investigation by the radiologist.

CT colonography has one unique imaging capability over all other current CRC screening methods. It offers the view of the entire abdominal and pelvic contents, therefore it allows for the identification of incidental extracolonic pathology. The impact of these findings has been under recent debate. Extracolonic findings offer the opportunity for early detection and treatment of potentially life threatening disease, such as abdominal masses or aortic aneurysm, in

healthy patients that may not have had imaging otherwise (Gryspeerdt & Lefere, 2006). This provides an additional benefit for use of CT colonography.

On the other hand, the identification of more benign extracolonic findings, such as granulomas, hernias, calcifications or cysts, may lead to skyrocketing costs for further follow-up investigation, additional radiation exposure, and unnecessary patient anxiety in otherwise healthy patients (Gryspeerdt & Lefere, 2006). Many radiologists worry about the ethical dilemmas these extracolonic findings pose. The ethical, health, and economic impact of extracolonic findings in CT colonography continues to be under much debate, and experts continue to search for a balance between the risks and benefits associated with such findings.

Research hypothesis

As the rates of colon cancer continue to be high and colon cancer screening continues to be low, much attention has been placed on finding the best methods for detecting CRC and improving patient testing compliance rates. With its recent inclusion in the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology's 2008 CRC screening recommendations, CT colonography has begun to gain more widespread acceptance and use in the medical community. Advancements in medical equipment and procedure methods have led to increased use of CT colonography as a means of detecting adenomatous polyps and cancer in instances when colonoscopy cannot be performed. Recently, however, there has been increased interest in whether or not CT colonography will become the primary method of CRC screening in place of standard colonoscopy for use in asymptomatic, average risk adults. It is the aim of this study to present current research addressing this issue. The research question to be investigated in this study is can CT colonography replace standard colonoscopy as a primary screening method for CRC?

Methods

An article addressing CRC screening guidelines and methods for screening for CRC was used to establish the criteria by which a screening test is deemed effective (Winawer et al., 2003). The authors of this article suggest important characteristics of an effective CRC screening test include accurately detecting the disease in its early stage, being established as a cost effective method, and being well accepted by the appropriate screening population. These three criteria were used to assess CT colonography in this project. A literature review was completed using searches performed on PubMed, the Mulford Library catalog, Ohiolink, and Google to find information on CRC, CRC screening, and CT colonography. A search on PubMeb for accuracy of CT colonography versus colonoscopy, cost effectiveness of CT colonography versus colonoscopy, and patient acceptance of CT colonography versus colonoscopy was performed to address the research question. Articles included in this paper are studies addressing CT colonography use in average-risk, asymptomatic individuals. Articles of studies completed on high risk patients were excluded from this paper, as screening is not appropriate in this population. Instead, individuals at high risk undergo more rigorous diagnostic testing. Studies from 1994 to the present were used in this paper to demonstrate advancements and improvements made in CT colonography since its development. These studies help to demonstrate why CT colonography has recently become more widely accepted. Articles in a language other than English were excluded from this study.

Discussion

Accuracy

For a test method to be deemed appropriate for widespread screening, the test must demonstrate the ability to successfully identify abnormalities for which it is testing. In the case of CRC screening, the test method must demonstrate the ability to identify adenomatous polyps that possess the potential to develop into cancer. For CRC screening methods, accuracy is measured by sensitivity and specificity of the test for identifying polyps. Sensitivity refers to the ability of a test to correctly identify those who have a condition, while specificity refers to the ability to correctly rule out those who do not have a condition.

Most studies of current CRC screening methods focus on sensitivity and specificity for identifying the advanced adenoma. As mentioned previously, advanced adenoma refers to a polyp greater than 10 mm in size, having high-grade dysplasia or is histologically villous in nature (O'Brien, et al., 1990). Large polyps have the highest likelihood of advancing to CRC, and therefore are considered the focus of CRC screening. Referral for polypectomy is always warranted when an advanced adenoma is found.

An area of concern with CT colonography is exposure to radiation associated with its use. A recent focus in CT colongraphy development has been on reducing exposure to radiation, while continuing to maintain a quality image that allows for accurate detection. A study of CT colonography using reduced radiation levels in a single-detector scanner found accuracy of polyp identification is not significantly affected when using a reduced radiation dose (van Gelder, et al., 2002). Despite inferior image quality and image reading time, the sensitivity and specificity using low dose CT remained high at 90% for adenomatous polyps 10 mm and over. The results

of this study suggest using low dose CT scanning will help to limit exposure to radiation without compromising accuracy.

Since the previous study, the clinical use of multi-detector CT scanners has become more widely accepted. The advantages of using multi-detector over single-detector helical scanners for CT colonography are reduced respiratory artifact, faster imaging in a single breath hold, and improved imaging quality from thinner slicing (Hara, et al., 2001). The scanning time using multi-detector scanners is significantly reduced. An early study evaluating CT colonography accuracy using multi-detector scanners demonstrated good sensitivity and specificity for lesions 10 mm and over when compared with standard colonoscopy; however, sensitivity and specificity were significantly reduced for lesions less than 10 mm (Gluecker, et al., 2002).

More recent studies of multi-detector scanners have shown better sensitivity results for detecting lesions smaller than 10 mm. Studies using lower-dose multi-detector row helical CT colonography resulted in significantly improved sensitivity for polyps 6 mm and over, with 100% sensitivity for polyps 10 mm and over, and between 81 and 86% sensitivity for polyps 6 to 9 mm (Iannaccone, et al., 2005; Wessling, et al., 2005). Both studies found these results to be comparable with or better than those found by standard colonoscopy. The studies also identified good specificity of CT colonography for lesions 10 mm and over; however, the specificity tended to decrease with smaller lesions. Specificity for lesions 10 mm and over was found to be 98%, while specificity for lesions 5 mm and less was found to be 87% (Wessling, et al.). Mistaking stool for polyps was identified to be the most common cause of false positives. Current practice guidelines established by the American College of Radiology advise using multi-detector scanners for CT colonography (American College of Radiology, 2006). The

improved accuracy with the use of multi detector scanners provides support for the possible widespread use of this method in a screening population.

The accuracy of CT colonography for detection of adenomatous polyps in the colon has been under debate since it was first introduced. Most early studies have evaluated the accuracy and use of CT colonography in high risk populations. More recently, there has been a larger focus on investigating the use of CT colonography as a screening tool in an asymptomatic, average risk population. Studies on this population have been carried out at centers of excellence throughout the country. The results of studies in asymptomatic, average risk populations, in which prevalence of the disease is generally low, identifies the appropriateness of the test for use as a primary screening method.

The first large study of the accuracy of CT colonography compared 96 average risk, asymptomatic patients with 204 high risk, symptomatic patients (Yee, et al., 2001). The authors used standard colonoscopy as a reference standard for both groups. They found sensitivity for detection of clinically important polyps 10 mm and over to be similar for both groups and significantly comparable with standard colonoscopy. Results for specificity of CT colonography were not as optimal. CT colonography identified 185 false positive polyps. Most false positive polyps were less than 10 mm, but this could lead to many unnecessary colonoscopy referrals if all polyps are referred for colonoscopy evaluation. The authors identified most false positive lesions in areas of poor distention and/or poorly cleansed areas of the bowel. The results support the importance of proper bowel preparation to maintaining good accuracy of findings in CT colonography.

Support for CT colonography as a widespread screening method has grown as studies have shown more encouraging results in identifying the presence of advanced adenomas in

average risk, asymptomatic patients. A large multi-center study by Pickhardt and colleagues (2003) found sensitivity and specificity of CT colonography for polyps 10 mm and over to be 93.8% and 96.0%, respectively. CT colonography surpassed standard colonoscopy in this study, whose sensitivity was 87.5% for polyps 10 mm or greater. The authors determined most polyps missed by colonoscopy and found by CT colonography were located behind haustral folds. It is important to note that the authors did use fecal tagging during preparation for CT colonography, a method not routinely accepted for use today.

Several additional studies also found similar supportive results. Macari and colleagues (2004) found CT colonography to have good sensitivity for polyps 10 mm or over, but only 56% of colonic lesions 6 to 9 mm found on colonoscopy were identified on CT colonography. With histological analysis of the "missed lesions", however, it was determined that five of eight of these lesions were actually benign normal mucosal protrusions, hyperplastic polyps, or ulcers and not polyps or cancer. This indicates that the actual sensitivity of CT colonography was 75% for lesions of this size, and contests the specificity of colonoscopy. One actual polyp 6-9 mm missed on CT colonography in this study was an adenoma at the dentate line. The authors suggest using a digital rectal exam in conjunction with CT colonography due to a limited ability to distend the lower rectal area.

Kim, Pickhardt, Taylor and colleagues (2007) also offer support for use of CT colonography for CRC screening because it offers similar accuracy rates as colonoscopy for advanced adenomas without the potential adverse effects. The authors compared a CT colonography and colonoscopy screening program of 3120 patients at a single institution and found both identified the same number of advanced adenomas in the patient population, but CT colonography resulted in less referrals to colonoscopy for polypectomies for lesions less than 10

mm in size. Surveillance for polyps 6 to 9 mm in size was used in the CT colonography group. The authors determined polypectomies performed for these lesions found by CT colonography yielded very few advanced lesions but resulted in the complication of colonic perforation in seven patients. The authors believe use of surveillance for polyps 6 to 9 mm is validated in this study due to limited clinical benefit obtained from their removal. They propose CT colonography is a safe and effective screening method that would offer more selective use of colonoscopy resources (Kim, Pickhardt, Taylor, et al.).

Studies by Johnson and colleagues (2008) and Graser and colleagues (2008) offer the most recent support for use of CT colonography. Johnson and colleagues completed the first large scale multi-center study in asymptomatic, average risk adults known as the American College of Radiology Imaging Network (ACRIN) National CT Colonography Trial. The study involved more than 2500 participants at 15 different centers. The authors found a sensitivity of 90% for advanced adenomas and cancers. Sensitivity for polyps 6 to 9 mm ranged from 78% to 90%, respectively. Despite high sensitivity, specificity in this study was low, ranging from 89% for small lesions to 86% for advanced adenomas. The authors believed the intense emphasis on polyp detection in radiologist training sessions was the cause. They support that specificity results would improve by increasing the threshold size for reporting. Using a 6 mm threshold for radiological reporting, instead of the 5 mm threshold they used, would improve specificity to 91% without affecting sensitivity, indicating lesions of this size are better able to be correctly identified. Use of a 6 mm threshold for referral to colonoscopy would also reduce the number of referrals to 12% from 17% using the 5 mm threshold. The authors support that the good accuracy with lower risk and less invasive nature of CT colonography in comparison with standard colonoscopy make it a potentially valuable screening tool. CT colonography has the

potential to increase compliance with CRC screening recommendations and reduce the number of unnecessary colonoscopies.

Graser and colleagues (2008) compared the accuracy of five different CRC screening methods. Results for CT colonography demonstrated a sensitivity of 91.3% and 92% for adenomas greater than 6 mm and greater than 10 mm, respectively. The sensitivity for colonoscopy was 97.8% for adenomas greater than 6 mm and 100% for 10 mm and greater. For patients with advanced neoplasia, CT colonography identified 96.7%, while colonoscopy identified 100%. The authors support colonoscopy as the most accurate means of screening for CRC; however, they suggest that poor rates of compliance with screening indicate the need for alternatives more appealing to the screening population. The results of their study suggest that CT colonography is a competitive alternative due to its good accuracy and limited invasiveness.

Not all studies offer such positive support for the use of CT colonography for CRC screening. Cotton and colleagues (2004) found CT colonography to have significantly poorer accuracy for advanced adenomas than standard colonoscopy. Overall sensitivity and specificity for lesions greater than 6 mm found on CT colonography was 39% and 90.5%, respectively, and 99% and 100% for standard colonoscopy. For polyps 10 mm and greater, sensitivity and specificity of CT colonography was 55% and 96%, respectively. The authors identified poor reader accuracy as the primary reason for poor results. Due to this, they suggest CT colonography is currently not ready to be used routinely or extensively. The authors advise that significant initial and ongoing radiologist training and feedback may be required for accurate reading. Despite this, they encourage that ongoing technology and technique advancements in CT colonography may improve its accuracy and validate its widespread use.

Accuracy for detecting advanced adenomatous polyps continues to be the most significant factor affecting the widespread utilization of CT colonography. Recent studies using newer and more advanced imaging techniques and use of this method as a screening tool in asymptomatic, average risk patients have continued to show positive support for identifying advanced adenomas. Demonstration of good accuracy in the asymptomatic, average risk population makes its potential use as a screening tool valid; however, proper training on this method is required ensure that radiologists have the necessary skills to accurately identify significant lesions found on CT images.

Cost Effectiveness

Whether or not a screening strategy is cost effective has a big impact on its reimbursement, and subsequently its implementation in mainstream health care. Many factors contribute to whether or not a CRC screening strategy is cost effective, including patient compliance, costs associated with the test, accuracy for a test to identify adenomatous polyps, and benefits obtained from identifying those polyps (Vijan, Hwang, Hofer, & Hayward, 2001). To be considered cost effective, the benefits of using a screening method must outweigh its risks.

Screening for CRC has been shown to identify potentially dangerous polyps early and thereby reduce mortality from advanced disease. Screening for CRC, therefore, offers a unique opportunity to prevent cancer. A study evaluating screening versus no screening found that screening for CRC has the potential to save over 31,000 lives every year if every person over the age of 50 years received it (Maciosek, Solberg, Coffield, Edwards, & Goodman, 2006). At current rates of CRC screening use, approximately 11,000 lives are saved every year (Maciosek, et al.). These statistics demonstrate that CRC screening has the potential to be highly effective at reducing CRC rates.

Maciosek and colleagues (2006) also evaluated cost effectiveness of screening versus no screening. They defined the cost effectiveness ratio as the total cost of screening and follow up minus costs saved on resources for treating advanced disease divided by the number of life year saved. The remaining figure is cost per life year saved. Their research found the average cost for CRC screening to be $11,900 per life year saved, which is well below the national levels for other accepted cost effective screening tests, such as mammograms. The results of this study support findings of a previous study by Vijan and colleagues (2001) that screening by any method is both beneficial and economical in preventing CRC.

While screening for CRC has been shown to be more cost effective than no screening, many studies have aimed to compare various methods of screening. With the recent increased focus on CT colonography as a potential widespread screening method, its ability to be a cost effective alternative has been in question. Several studies have addressed the cost effectiveness of this method in comparison with standard colonoscopy, as well as other screening methods. For this study, only results comparing CT colonography versus colonoscopy will be mentioned.

Accuracy for identifying polyps plays a major role in the cost effectiveness of CT colonography when compared with standard colonoscopy. An early study by Sonnenberg, Delco, and Bauerfeind (1999) reported CT colonography is less expensive than standard colonoscopy on a procedural basis, but it is more costly overall due to the costs associated with cancer treatment for missed polyps. Ladabaum, Song, and Fendrick (2004) also report the decreased sensitivity of CT colonography for identifying all adenomas present decreases its cost effectiveness. They state the cost effectiveness would be comparable with standard colonoscopy if the sensitivities of both tests were the same.

Costs associated with the procedure and its follow up significantly impact the cost effectiveness of a screening tool. Costs associated with CRC screening include cost of the procedure, follow up, treatment for cancer, treatment of complications, and indirect costs, such as time off work. In studies comparing the overall cost effectiveness between CT colonography and colonoscopy, costs were estimated from a third party payer perspective using CPT codes. Charges using CPT codes for abdominal CT were used to determine the costs associated with CT colonography due to a lack of specific coding for this procedure. It is important to note that current insurance regulations no longer allow for charging using abdominal CT codes for CT colonography in clinical practice.

Study results comparing cost effectiveness of CT colonography versus standard colonoscopy were varied. Despite these varied results, all studies found CT colonography to be more effective and cost efficient than no screening (Ladabaum, et al., 2004; Pickhardt, Hassan, et al., 2007; Sonnenberg, et al., 1999; Vijan, et al., 2007). Three studies found CT colonography to be a considerably more costly method than standard colonoscopy. Sonnenberg and colleagues estimated a CT colonography program to prevent CRC is more expensive than a standard colonoscopy program. They determined a 15-20% increase in patient compliance or a cost 54% less than standard colonoscopy would be required for CT colonography to be competitively cost effective. Ladabaum and colleagues and Vijan and colleagues also found CT colonography to be more costly than standard colonoscopy. They estimated that CT colonography would need to cost 60% less than standard colonscopy to make it competitive. All three of these studies assumed that all adenomatous polyps found on CT colonography would be referred to standard colonoscopy, a practice not commonly used today.

Two recent studies reported more promising results. These studies compared the cost effectiveness of CT colonography using a reporting threshold of 6 mm with standard colonoscopy. In these studies, any polyps found on CT colonography to be 5 mm or less were not reported, and therefore not referred to colonoscopy. This follows The Working Group on Virtual Colonoscopy's current recommendations that polyps less than 6 mm should not be reported due to their clinical insignificance and minimal risk for CRC (Zalis, et al., 2005).

Pickhardt, Hassan and colleagues (2007) found CT colonography using a 6 mm threshold to be the safest and most cost effective method of CRC screening. Use of a 6 mm threshold of reporting resulted in a savings of almost $5000 per life year over standard colonoscopy and a 77.6% reduction in invasive procedure use. The authors determined that reporting polyps less than 6 mm resulted in significant and unnecessary financial burden and offered minimal clinically relevant gain.

The cost effectiveness of using a threshold for reporting was also supported by Lansdorp-Vogelaar and colleagues (2009). The authors determined that CT colonography is more cost effective than standard colonoscopy when using a 6 mm threshold, with screening at 5 year intervals, and while maintaining a 60% lower cost. They report, however, the cost effectiveness of CT colonography using a threshold of 6 mm is reliant on the expertise of the radiologist to correctly measure polyps. Errors in reading size can cause an incorrect referral. The authors believe the error is more likely to favor a more intensive referral for polyps found; however, this significantly reduces the cost effectiveness of this method.

While a 6 mm threshold of reporting has been shown to be the most financially beneficial, the most cost effective action for polyps 6 to 9 mm has also been under much debate. Current recommendations for clinical practice support immediate polypectomy of any polyps 6

mm or greater (Levin, et al., 2008); however, this may cause unnecessary financial costs with little clinical benefit. As mentioned earlier, most lesions of this size have been found to be benign (Aldridge & Simson, 2001; Shinya & Wolff, 1979).

The Working Group on Virtual Colonoscopy has provided clinical recommendations to serve as a consensus for reporting all adenomatous polyps found on CT colonography called the CT Colonography Reporting and Data System. They recommend patients with one or two polyps 6 to 9 mm be followed by surveillance with CT colonography every 3 years (Zalis, et al., 2005). Despite these recommendations, the authors conclude that follow-up should be determined on an individualized patient basis, and patients with three or more polyps should always be referred to colonoscopy for polypectomy.

Several studies have investigated the cost effectiveness of recommended surveillance of polyps 6 to 9 mm. Pickhardt and colleagues (2008b) determined the estimated 10-year risk of CRC to be 0.7% for polyps 6 to 9 mm, but the costs associated with removing all such polyps were high. It was found that 297 polypectomies would have to be performed in this size group for prevention of one CRC to occur. The authors report the relatively low medical gain and the high associated cost with removal of all polyps 6 to 9 mm suggests that surveillance of these polyps is more beneficial and cost effective.

In an additional study, Pickhardt and colleagues (2008a) also found polypectomy of polyps 6 to 9 mm in size to be both expensive and of little clinical benefit. Immediate polypectomy leads to significantly higher screening costs, and endoscopic complications outweigh clinical benefits obtained by removal of such polyps. They agree with previous studies that the most cost effective action for polyps 6 to 9 mm is short term surveillance by CT colonography every 3 years.

Patient compliance with CRC screening recommendations also directly influences the cost effectiveness of screening. When more individuals comply with screening recommendations, the cost effectiveness of the screening method increases. Several studies suggest that if offering CT colonography as a screening method improves patient compliance with screening, it will be a comparable to colonoscopy as a cost effective screening tool (Ladabaum, et al., 2004; Pickhardt, Hassan, et al., 2007; Sonnenberg, et al., 1999).

The most significant issue in support for the cost effectiveness of CT colonography is that it will allow a better allocation of health care resources by reducing the number of colonoscopies performed. A study using quantitative mathematical modeling estimated a 20% reduction in colonoscopies with widespread CT colonography screening using a 10 mm threshold for polypectomy (Hur, Gazelle, Zalis, & Podolsky, 2004). Results of an actual 3 year CT colonography screening program at the University of Wisconsin, however, found the number of diagnostic or therapeutic colonoscopies performed did not decrease with CT colonography use (Schwartz, et al., 2008). Despite these results, polypectomy after CT colonography for polyps 6 mm and over did not result in an increase in therapeutic colonoscopies performed at this facility. The authors suggest CT colonography offers an additional method of screening for CRC, but it does not affect the need for colonoscopy. They advise that further studies using community-based screening programs and stricter colonoscopy referral are needed to determine the full effect of CT colonography on use of colonoscopy resources.

Whether or not CT colonography is a cost effective screening method has great bearing on its reimbursement in today's health care environment. In comparison with no screening, CT colonography has been found to be cost effective by preventing costs associated with treating cancer. In comparison with standard colonoscopy, results studying the cost effectiveness of CT

colonography have varied. CT colonography proves to be more cost effective when the threshold for referral to polypectomy is increased. Using a threshold limits unnecessary costs associated with polypectomy for insignificant lesions. If the costs associated with CT colonography remain low and accuracy and patient acceptance remain high, CT colonography has a very good potential for being a significant cost effective method of screening for CRC.

Patient Acceptance

While accuracy and cost effectiveness are both essential to validating a CRC screening method, patient acceptance of the method has the potential to make the most significant impact on its widespread use. Nearly 42 million people of the recommended age are not getting screened for CRC (Seeff, et al., 2004). Despite all findings supporting the effectiveness of CRC screening in preventing cancer, statistics show the use of current CRC screening methods is low (Shapiro, et al., 2008). This lack of widespread acceptance of currently available screening tests indicates a need for a test which people are willing to use. CT colonography has been proposed to be a more patient-friendly CRC screening method, and its potential to improve compliance with CRC screening recommendations is currently being investigated.

Due to its lack of widespread use as a screening method, knowledge concerning acceptance of CT colonography by patients in the average risk screening population is limited. Most studies addressing patient acceptance have been in high risk populations, the population in which it has most commonly been used. To date, four studies have compared acceptance of CT colonography with standard colonoscopy in a primarily average risk population. These studies used questionnaires to compare patient experiences with both CT colonography and colonoscopy.

Thomeer and colleagues (2002) were the first to examine patient acceptance of CT colonography in comparison with colonoscopy using patients of a screening population. This study's population was mixed with patients seeking primary screening, or average risk patients, and screening for follow-up on symptoms or positive findings on previous colonoscopy; therefore, it was not a pure study of asymptomatic, average risk patients. Regardless of this fact, the authors found 88 of 124 of patients in their study preferred CT colonography. Patients cited reduced procedural time, lack of sedative use, and easier testing procedures as the most common reasons. No statistical significance in discomfort between tests was found; however, the authors believed sedative use in colonoscopy may have affected perceived patient discomfort during this procedure. They suggest that CT colonography is a more accepted CRC screening procedure than standard colonoscopy.

Three additional studies assessing the acceptability of CT colonography found similar results to Thomeer and colleagues (2002). Edwards and colleagues (2004) found CT colonography to be well accepted by patients in an average risk, asymptomatic community-based population. Sixty-one percent of subjects in their study reported positive experiences with the test and agreed they would repeat the test again if offered. Juchems and colleagues (2005) identified a statistically significant preference for CT colonography over standard colonoscopy in an average risk screening population. They identified this preference is most likely due to a decreased recovery time required by CT colonography. Scott and colleagues (2004) also found acceptability of CT colonography to be high; however, no statistically significant difference between CT colonography and colonoscopy was found. In all three studies, participants identified bowel preparation as the most difficult and unpleasant portion of both tests.

Information on patient acceptance of CT colonography is scarce due to its limited widespread use. Preliminary studies suggest that patients are highly accepting of CT colonography for CRC screening and would agree to utilize this technique. This acceptance indicates that CT colonography could have a positive impact on the large deficit in CRC screening. Until CT colonography becomes more accessible, however, its true impact on patient utilization of CRC screening cannot fully be determined.

Conclusion

Colorectal cancer is a significant and deadly health problem that affects many people in this country every year. It arises from multiple and specific genetic mutations in cells of the colonic mucosa. The mutations lead to growths, called adenomatous polyps, on the mucosal epithelial surface. Advanced adenoma is the term given to a polyp at the highest risk of developing into CRC. It is defined by a size greater than 10 mm, villous histology, or high-grade dysplasia (O'Brien, et al., 1990). Knowledge of the progression of adenomas to cancer has allowed for the unique opportunity to prevent CRC through screening. The goal of CRC screening is to identify high risk advanced adenomas and remove them before the change to CRC occurs.

Despite the effectiveness of screening for preventing cancer, many people of recommended screening age are not undergoing the appropriate screening. The lack of screening utilization provides an opportunity for physician assistants in the primary care setting to positively impact CRC screening rates. Physician assistants can provide patients with the education, encouragement, and information needed to seek complete CRC screening. In order to be able to do this effectively, physician assistants must maintain current knowledge of CRC screening recommendations and methods.

Several methods are currently available to use for CRC screening. Some methods, like the fecal occult blood test (FOBT), stool DNA test, and fecal immunochemical test, only screen for the presence of CRC. Other methods, such as flexible sigmoidoscopy, contrast barium enema, standard colonoscopy, and CT colonography, detect for adenomatous polyps and cancer by allowing structural viewing of the colon and are the methods most encouraged for screening (Levin, et al., 2008). Colonoscopy is currently the gold standard for CRC screening; however,

compliance with this method is low (Shapiro, et al., 2008). CT colonography is the newest recommended screening method. It is a minimally invasive method of screening for CRC that utilizes 2D and 3D computed tomography images of the entire colon to detect adenomatous polyps. Recent advancements in CT scanners, imaging software, and procedure techniques have led to increased interest into whether this method can be used for widespread CRC screening. The question proposed by much of the medical community and by this scholarly project is whether CT colonography can replace standard colonoscopy as a primary method of CRC screening in the average risk, asymptomatic population.

To be appropriate for widespread use as a screening method, a CRC screening method must be accurate for detecting advanced adenomas, demonstrate cost effectiveness, and be accepted by the population it screens (S. Winawer, et al., 2003). The gravitation toward use of multi-detector scanners has improved both sensitivity and specificity for polyp detection, but repeated exposure to radiation with long term use of CT colonography is a risk with this method (Iannaccone, et al., 2005; Wessling, et al., 2005). Even though study estimations have predicted that lifetime risks from radiation exposure in CT colonography are low (Brenner & Georgsson, 2005), the lack of investigation into this means the complete harm from exposure may not be fully known. It is important for physician assistants to inform patients of the risk when discussing this method.

The primary target of CRC screening is the advanced adenoma due to its significant risk of progression to cancer. Sensitivity of CT colonography for detection of advanced adenomas in an average risk screening population has been found to be comparable to or better than standard colonoscopy in many studies (Johnson, et al., 2008; Kim, Pickhardt, Taylor, et al., 2007; Macari, et al., 2004; Pickhardt, et al., 2003; Yee, et al., 2001). These results suggest that CT

colonography can reliably identify the presence of an advanced adenoma. Because CT colonography has comparable sensitivity to colonoscopy for advanced lesions and has less risks and complications associated with its use, it is an attractive alternative for an average risk population.

While sensitivity results of CT colonography provided support for it use, specificity results were not as positive. Poor specificity indicates that false positives are common with test use, and many patients are unnecessarily referred to colonoscopy. Unnecessary referral both increases the costs and patient burden when associated with this use, especially if a patient is unable to schedule the colonoscopy for the same day. Poor specificity has most commonly been found to be due to poor distention or bowel cleansing (Yee, et al., 2001). By focusing on educating the patient of the importance of bowel preparation, the occurrence of false positives and unnecessary colonoscopy may be reduced.

In addition, it has been suggested appropriate training for radiologists on CT colonography interpretation would improve specificity results (Cotton, et al., 2004; Johnson, et al., 2008). The need for radiologists with specific and intense training in the reading of CT colonography poses a limitation for widespread implementation of CT colonography screening programs. To be comparable with standard colonoscopy, the access to training must be made available to radiologists in all facilities with available CT scanners.

Due to its current limited widespread use in screening populations, it is difficult to determine the precise impact CT colonography will have on costs associated with CRC screening or patient adherence to CRC screening recommendations. CT colonography has been found to be more cost effective than no screening (Ladabaum, et al., 2004; Pickhardt, Hassan, et al., 2007; Sonnenberg, et al., 1999; Vijan, et al., 2007). As mentioned earlier, a large portion of this

country's population is not undergoing recommended CRC screening. Preliminary studies on the acceptance of CT colonography in an average risk screening population suggest patient acceptance of this method is high (Edwards, et al., 2004; Scott, et al., 2004), and often preferred over standard colonoscopy (Juchems, et al., 2005; Thomeer, et al., 2002). Results of these studies suggest that patients are likely to utilize and repeat CT colonography testing. With improved adherence, CT colonography may be more cost effective than currently underutilized standard colonoscopy.

CT colonography is a rapidly developing method of CRC screening that offers an accurate, well tolerated, and less invasive option for CRC screening. Comparing and contrasting it with standard colonoscopy is complex. Both methods have advantages and disadvantages that support its use in some populations and limit it in others. The complexity of CRC and the methods used to screen for it make it difficult to select one method as superior. The decision to undergo CRC screening is both an individualized and personal decision. Any method that promotes the use of CRC screening offers an invaluable opportunity to decrease mortality from this disease. It is, therefore, believed that CT colonography will not replace standard colonoscopy for CRC screening but instead will provide patients with an additional alternative in hopes that they make an active decision to get screened.

Physician assistants play an important role in this screening decision process. Communication between health care provider and patient about CRC screening has the biggest impact on whether or not a person makes the choice to get screened (Carcaise-Edinboro & Bradley, 2008). In order to do this, physician assistants must make a conscious effort to maintain current knowledge of CRC screening recommendations and screening methods. It is the responsibility of the physician assistant to seek out knowledge of CT colonography, its

reimbursement, its current availability, and the presence of CT colonography trained radiologists in their own community. By doing so, physician assistants will be able to assist their patients in making informed and autonomous decisions about CRC screening that could potentially save lives.

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Table 1

Screening Guidelines for the Early Detection of Colorectal Cancer and Adenomas: Tests that Primarily Detect Cancer

Test	Interval	Key Issues for Informed Decisions
gFOBT with high sensitivity for cancer FIT with high sensitivity	Annual Annual	• Depending on the test, 2 to 3 home stool samples needed for testing; a stool sample gathered by digital exam in office is not to be used for testing • Colonoscopy should be recommended if the tests results are positive • If the test is negative, repeat annually • One-time testing is likely to be ineffective
sDNA	Interval uncertain	• An adequate stool sample obtained and packaged with preservation agents required for shipping to laboratory • Cost is significantly higher than other forms of stool testing • If the test is positive, colonoscopy will be recommended • If the test is negative, repeat test interval is uncertain

Abbreviations: gFOBT, guaiac-based fecal occult blood test; FIT, fecal immunochemical test; sDNA, stool DNA test.

Note. From "Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: A joint guideline from the America Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology" by Levin et al., 2008, CA, 58, p. 135.

Table 2

Screening Guidelines for the Early Detection of Colorectal Cancer and Adenomas: Tests that Detect Adenomatous Polyps and Cancer

Test	Interval	Key Issues for Informed Decisions
FSIG with insertion to 40 cm or splenic flexure	every 5 years	• Complete or partial bowel prep required • Sedation often not used, so there may be discomfort • Protective effect is limited to portion of colon examined • Positive findings will lead to referral to colonoscopy
Colonoscopy	every 10 years	• Complete bowel prep required • Conscious sedation used in most centers: patient will miss a day of work and will require transportation home • Rare but serious risks include perforation and bleeding • Risks mostly associated with polypectomy
DCBE	every 5 years	• Complete bowel prep required • If 1 or more polyps > 6 mm found, colonoscopy required • Risks are low; rare cases of perforation have been reported
CTC	every 5 years	• Complete bowel prep is required • If 1 or more polyps > 6 mm, colonoscopy recommended (if alternate day, additional bowel prep required) • Risks are low; rare cases of perforation have been reported • Extracolonic abnormalities found may require further evaluation

Abbreviations: FSIG, flexible sigmoidocsopy; DCBE, double contrast barium enema; CTC, computed tomography colonography

Note. From "Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: A joint guideline from the America Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology" by Levin et al., 2008, CA, 58, p. 135. Adapted with permission of the author.

Table 3

Protocol for Polyps Identified on CT Colonography Screening

Adenomatous Polyp Size	**Proposed Action**
10 mm or greater	Immediate referral to colonoscopy
Greater than 2 polyps 6-9 mm in size	Immediate referral to colonoscopy
Less than 2 polyps 6-9 mm in size identified	Patient choice (removal versus surveillance of every year for polyps 8-9 mm, or every two years for polyps 6-7 mm)
5 mm or less	No action taken

Note. Compiled from information found in "Computed tomographic colonography for colorectal screening" by Kim, D.H., Pickhardt, P.J., Hoff, G., & Kay, C.L., 2007, Endoscopy, 39, p. 545.

Abstract

Introduction: Colorectal cancer (CRC) is a common and preventable cancer. Currently, several methods exist for CRC screening, including computed tomography. CT colonography is a new, minimally invasive technique for examining the entire colon using CT imaging. It is the aim of this study to present current research on CRC screening and investigate whether CT colonography could be a primary screening method for CRC.

Methods: Literature searches on PubMed, the Mulford Library catalog, Ohiolink, and Google were used to research CRC, CRC screening, and CT colonography.

Discussion: The sensitivity of CT colonography for advanced adenomas is comparable to or better than standard colonoscopy. Due to limited use in screening populations, the widespread cost effectiveness and acceptance of CT colonography is difficult to determine. Preliminary studies have shown good results.

Conclusion: CT colonography provides a promising alternative for CRC screening in hopes that more patients will choose to undergo screening.