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The role of virtual colonoscopy in colorectal screening

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ABSTRACT

Colorectal cancer is the second leading cause of cancer-related deaths in the United States. The earlier colorectal cancer is detected, the better chance a person has of surviving 5 years after being diagnosed, emphasizing the need for effective and regular colorectal screening. Computed tomographic colonography has repeatedly demonstrated sensitivities equivalent to the current gold standard, optical colonoscopy, in the detection of clinically relevant polyps. It is an accurate, safe, affordable, available, reproducible, quick, and cost-effective option for colorectal screening and should be considered for mass screening.

1. Colorectal cancer epidemiology

Colorectal cancer is the third most common cancer diagnosed in men and women in the United States. For the year 2015, the American Cancer Society (ACS) estimates 93,090 new cases of colon cancer and 39,610 new cases of rectal cancer, resulting in approximately 49,700 deaths in the United States [1]. It is the third leading cause of cancer-related deaths in the United States when men and women are considered separately, and the second leading cause when both sexes are combined. Based on data collected from 2009 to 2011 by the National Cancer Institute, it is estimated that the lifetime risk of developing colon cancer is approximately 4.7%, with an average 5-year survival rate of 64.7% [1,2].

2. Colorectal cancer pathophysiology

Virtually all colon cancers arise from polyps. Even though there are individuals who are prone to developing polyps such as individuals with a personal or family history of colorectal cancer, individuals with inflammatory bowel disease, or individuals with hereditary forms of colorectal cancer, 75%–95% of all colon cancers develop in individuals with little or no genetic predisposition for malignancy.

There are two key models or pathways proposed for colorectal cancer development. The vast majority of colorectal cancers arise from mucosal epithelial cells, which undergo a series of mutations according to a well-established adenoma–carcinoma sequence. In this pathway, colorectal cancers arise from precursor lesions known as adenomatous polyps, which undergo a series of stepwise mutational activation of oncogenes and inactivation of tumor suppressor genes, resulting in an abnormal process of cell proliferation and apoptosis, ultimately leading to carcinoma [3].

The risk of colon cancer increases with the number of adenomatous polyps. The overall prevalence of adenomas in the general population is estimated at 30%–50% and increases with age. It is approximated that 1%–3% of these adenomas ultimately progress to cancer, with the risk increasing with lesion size. Majority of adenomas are less than 1 cm and frequently remain small, without cancerous transformation. Lesions that are 1 cm in size have approximately 1% incidence of harboring invasive cancer, while those that are greater than 1 cm have approximately 10% chance of containing cancer or 25% chance of progressing to cancer over a 20-year time period [4,5]. In addition to size, histologic growth pattern also influences the likelihood of an adenoma containing cancer. There are 3 main growth patterns—tubular, tubulovillous, and villous—of which villous has the highest propensity for malignant growth.

More recently, a serrated neoplastic pathway for colorectal carcinogenesis has also been identified, accounting for approximately one third of all colorectal cancers [6]. Serrated lesions are a group of polyps that can be classified pathologically according to the World Health Organization as hyperplastic polyps, sessile serrated adenoma/polyps, or traditional serrated adenomas. While most hyperplastic polyps are typically benign, small subsets, particularly large hyperplastic polyps in the right colon, have been shown to be precursors to sessile serrated adenomas, which can ultimately progress to cancer themselves. While both sessile serrated adenomas and traditional serrated adenomas are considered premalignant lesions, sessile serrated adenomas represent the dominant precursor to colorectal cancer development in this pathway.

3. Colorectal staging

With an appropriate emphasis on colorectal screening, we are now detecting polyps at an early stage and removing them far before they

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develop into cancers. Through effective, regular screening, we are able to diagnose colorectal cancer approximately 2–3 years earlier than diagnosis of cases with symptoms [7]. This is particularly important as prognosis is intimately related to patient's staging at the time of diagnosis.

The TNM staging system established by the American Joint Committee on Cancer is the most widely used staging system for colorectal cancer. This system essentially evaluates three key components in determining staging of the cancer, as follows:

T: indicates how invasive the primary tumor is and degree of extension into the wall of the intestine and surrounding structures.
N: indicates the extent of spread to regional lymph nodes.
M: indicates whether the cancer has metastasized to other organ systems.

According to the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, at the time of diagnosis, 39.6% of individuals have local stage disease, confined to the primary site, with an average 5-year survival of 89.8%. Thirty-six percent of individuals are diagnosed in the regional stage, with spread of disease to regional lymph nodes, and have a 5-year survival rate of 70.5%. Twenty percent are diagnosed with distant metastasis with a 5-year survival rate of 12.9%, and 5% are unstaged at time of diagnosis with an average 5-year survival rate of 33.2% [1].

4. Colorectal screening

The earlier colorectal cancer is detected, the better chance a person has of surviving 5 years after being diagnosed, emphasizing the need for accurate, safe, reliable, cost-effective colorectal screening. The ACS recommends screening beginning at the age of 50 years old in asymptomatic men and women at average risk for developing colorectal cancer. High-risk patients, those with either a personal or family history of high-risk conditions, should obtain screening at an earlier stage. These high-risk conditions include a personal history of prior colonic adenomatous polyps, prior colon cancer, Peutz–Jeghers syndrome, hereditary nonpolyposis colorectal cancer (HNPCC), juvenile polyposis syndrome, or chronic inflammatory bowel disease. In addition, a family history of colon cancer, colonic adenomatous polyps, HNPCC, or familial adenomatous polyposis (FAP) also categorizes a patient as high risk, and screening is tailored on an individual basis.

For patients with a family history of colorectal cancer or adenomatous polyps in first-degree relatives aged <60 years or colon cancer in two or more first-degree relatives at any age, the ACS recommends screening starting at age 40 or 10 years before the youngest index case, whichever is earlier. For those with family members with a history of colon cancer at age >60 years, screening is recommended at age 40 years. Among the earliest age recommendations for colorectal cancer screening is age 10–12 years for individuals with FAP and age 20–25 years or 10 years before the youngest case in the immediate family of individuals with HNPCC.

There are a number of colorectal screening tests available, which can be divided into cancer prevention and cancer detection tests. Cancer prevention tests have the potential to image both cancer and polyps, whereas cancer detection tests have lower sensitivity for polyps and typically lower sensitivity for cancer detection [8,9].

4.1. Tests that detect polyps and cancer:

Colonoscopy—recommended every 10 years.
Computed tomographic colonography (CTC; virtual colonoscopy)—recommended every 5 years.
Flexible sigmoidoscopy—recommended every 5 years.
Double-contrast barium enema—recommended every 5 years.

4.2. Tests that detect cancer:

Guaiac-based fecal occult blood test—recommended every year.
Fecal immunochemical test—recommended every year.
Stool DNA test—recommended every 3 years.

Colorectal cancer is a preventable condition with proper screening; however, adherence to a regular schedule has posed a major hurdle. The "ideal" screening test should meet several criteria as screening exposes healthy asymptomatic individuals to testing with potential for harm. It should be accurate, safe, affordable, available, reproducible, quick, and cost-effective for society as a whole.

Optical colonoscopy has traditionally been used as the examination of choice for colorectal cancer screening as an intervention can be performed at the time of screening. Optical colonoscopy, however, has several disadvantages as a screening test. It is resource intensive, invasive, and often uncomfortable, discouraging patients from obtaining regular screening. In many settings, optical colonoscopy requires sedation and possibly analgesia, requiring the presence of an anesthesiologist and postprocedural monitoring. In addition, although small, there is a risk for perforation and bleeding, with an overall complication rate of approximately 0.4% [10].

5. Role of CTC

CTC, also called virtual colonoscopy, has emerged as an alternative to the traditional gold standard, optical colonoscopy, for screening asymptomatic adults and is considered the best radiological diagnostic test for imaging colorectal cancer. CTC is a minimally invasive alternative to optical colonoscopy for total colonic colorectal evaluation and has considerable potential for widespread screening. In 2008, the ACS guideline for colorectal cancer screening was revised jointly with the US Multi-Society Task Force on Colorectal Cancer and the American College of Radiology (ACR) to include CTC every 5years as an option for screening average-risk individuals. CTC has repeatedly demonstrated sensitivities equivalent to those of optical colonoscopy in the detection of clinically relevant polyps. A large prospective study performed by Pickhardt et al. demonstrated that virtual colonoscopy compares favorably to optical colonoscopy. Sensitivity of virtual colonoscopy for adenomatous polyps was 94% for polyps at least 10 mm in diameter, 94% for polyps at least 8 mm in diameter, and 89% for polyps at least 6 mm in diameter. Similarly, sensitivity of optical colonoscopy for adenomatous polyps was 88%, 92%, and 92% for the three size categories of polyps, respectively. The specificity of virtual colonoscopy for adenomatous polyps was 96% for polyps at least 10 mm in diameter, 92% for polyps at least 8 mm in diameter, and 80% for polyps at least 6 mm in diameter [11]. This study was further validated by a multicenter prospective study performed by Johnson et al, which demonstrated CTC sensitivity of 90% for adenomas measuring 10 mm or more [12]. Large systematic review and meta-analyses have also upheld comparable sensitivities between CTC and optical colonoscopy, despite variations in CTC protocols among different institutions [13].

Multiple further analyses of the efficacy of CTC in the Medicare population 65 years and older have also shown equivalent efficacy in this age group compared to larger previous trials [14–17]. Comparison of outcomes for CTC versus optical colonoscopy in the pathologic yield of advanced neoplasia has demonstrated equivalent detection rates with significantly lower polypectomy and complication rates in the CTC screening group [18].

There are several potential advantages and benefits of CTC over optical colonoscopy. Compared to traditional optical colonoscopy, there is no need for sedation, and patients are able to avoid the cardiopulmonary risks associated with anesthesia. In addition, virtual colonoscopy requires less technical staff as it can be performed without the presence of anesthetists and nurses. It is a fast examination, requiring approximately 10–15 min of table time. Patients are able to stay