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Colorectal Cancer

Introduction

In 2008, colorectal cancer ranked 3rd among the most incident forms of nonskin cancer in the U.S. for both men and women (1). Colorectal cancer is also one of the leading causes of cancer deaths; more than 50,000 Americans die each year of colon or rectal cancer (1), constituting a major public health concern. There are well established screening techniques in place that can help reduce the number of deaths caused by colorectal cancer each year (2). These procedures, however, are generally underutilized by the population at risk; in 2000, approximately 40% of adults aged 50 years and older reported that they had received a colon endoscopy within the past 5 years or a fecal occult blood test (FOBT) within the previous year (3). Additionally, those at risk for colorectal cancer may not have access to this type of preventative care. This chapter will describe, in detail, the risk factors associated with colon cancer, the types of screening tests available, and organizations that offer preventative services.

What is Colon Cancer?

The colon and rectum together make up the large intestine, part of the body's digestive system. The colon is a large muscular tube (approximately five feet long) that collects and stores waste which then passes into the rectum. Tumors can develop within the walls of the colon and/or rectum tissue which are called polyps (2). These tumors can either be malignant (cancerous) or benign. Benign polyps may develop into adenomatous polyps over time and in fact, about 85% of all colorectal cancers develop from adenomatous polyps (2). Note that colon

cancer and rectal cancer together are referred to as colorectal cancer.

Risk Factors

Epidemiologic studies have revealed a number of risk factors for colorectal cancer including age, family history of colon cancer or inflammatory bowel disease, smoking, alcohol consumption, obesity, and diet.

1. **Age**

Colorectal cancer is most commonly found in those aged 50 years and over. The SEER (Surveillance Epidemiology and End Results) Cancer Statistics Review found that between 1998 and 2002, less than 15% of new colorectal cancer cases occurred among those less than 54 years of age, 17% occurred among those between 55 and 64 years old, 26.3% occurred among those between 65 and 74 years old, 29.2% occurred among those between 75 and 84 years old, and 12.6% of new cases were among those over the age of 85 (4). When colon and rectal cancers are considered separately, over 50% of new cases in each group still occur among those 65 to 84 years old (4).

2. **Sex**

Men are more likely than women to develop colorectal cancer. The incidence rate of colorectal cancer between 2000 and 2004 was 69.2 per 100,000 population among men and 45.8 per 100,000 population among women (1). The SEER Review found similar incidence rates between 1998 and 2002. Additionally, the breakdown between the rates of colon and rectal cancers were given separately in that report. The incidence of colon cancer was 43.4 per

100,000 among men and 34.5 per 100,000 among women and the incidence of rectal cancer was 18.5 per 100,000 and 11.7 per 100,000 for men and women respectively (5).

3. Race

African Americans have the highest incidence rates of colorectal cancer. Between 2000 and 2004, the number of new cases of colorectal cancer per 100,000 population among men was 60.4 among whites, 72.6 among African Americans, 49.7 among Asian Americans and Pacific Islanders, 42.1 among American Indians and Alaska Natives, and 47.5 among Hispanics and Latinos (1). Among women during the same time period, the number of new cases of colorectal cancer per 100,000 population was 44.0 among whites, 55.0 among African Americans, 35.3 among Asian Americans and Pacific Islanders, 39.6 among American Indians and Alaska Natives, and 32.9 among Hispanics and Latinos (1).

4. Family History

According to the CDC (Center for Disease Control and Prevention), those who have a family history of colorectal cancer are at higher risk for developing colorectal cancer themselves (7). In addition to particular genetic pathways that are activated in the development of colon cancer, there are also known genetic mutations that can be inherited and make up approximately 10% of all colorectal cancer cases (8). One of these genetic mutations is called familial adenomatous polyposis (FAP), which causes hundreds or thousands of polyps to develop in the colon from a very young age (14). If these polyps are left untreated, that person has a very high risk of those polyps developing into cancer. Another genetic mutation that causes colorectal cancer is hereditary non-polyposis colorectal cancer (HNPCC) which accounts for 5%-8% of

colorectal cancers (8). Unlike FAP, HNPCC does not result in an excess number of polyps. According to Heavey, *et al*., HNCPP "seems to accelerate the carcinogenic process through an increased mutation rate in microsatellite regions, which then affects other genes involved in cell cycling and proliferation" (8). Someone with HNPCC has an 80% chance of developing colorectal cancer throughout his or her life (14). While other genetic mutations have been associated with increased colon cancer risk, those two (FAP and HNPCC) are the most common. While other factors also contribute to the development of colon cancer, understanding family history is an important first step in assessing an individual's risk.

5. Smoking

Tobacco use does not only put persons at risk for higher rates of lung, mouth, and esophageal cancers; it has also been associated with higher risk for developing colon cancer (7, 8, 15). A meta-analysis conducted by Botteri, *et al*. based on 42 observational studies found that current smokers were at a much higher risk of developing adenomatous polyps than those who had never smoked (OR = 2.14; 95% CI 1.86 – 2.46). In this study, former smokers and ever smokers had a higher risk of developing adenomatous polyps than never smokers which was also significant (16). Additionally studies have shown that smokers have a greater risk of recurrent adenomas than nonsmokers (8). The 2004 Surgeon General's Report gives a more detailed description of the studies that have examined the association between smoking and risk of developing colon cancer. The report also offers an in depth look at how carcinogens from cigarettes and other tobacco products are directly linked to cancer development. The report can be found online at: http://www.cdc.gov/tobacco/data_statistics/sgr/sgr_2004/#full.

6. Diet

There have been a number of different dietary factors that have been linked to a higher risk of colorectal cancer including higher levels of red meat consumption, low levels of fruit and vegetable consumption, and diets that are low in fiber (7, 8). Despite the fact that research on meat consumption and preparation techniques/doneness has been somewhat inconsistent, there seems to be fairly strong evidence that diets high in red meat are associated with an increased risk of colon cancer (8). One study in particular, conducted by Sinha et al., found that there was an increased risk of adenomatous polyps among those with a higher level of red meat intake and that this risk was even higher for those whose meat was cooked to well done or very well done (19). Other case-control studies have shown similar findings (8). Fruit and vegetable intake may be another important dietary factor that affects one's risk of colon caner. Recent findings from the European Investigation into Cancer (EPIC) study have shown that higher vegetable consumption is moderately associated with a decreased risk of colorectal cancer (8). In other studies, however, this protective association has not been significant. It seems that the most important dietary element in decreasing one's risk for colorectal cancer is fiber intake. A meta-analysis of 16 case-control studies conducted by Trock et al., found that diets high in fiber reduced the risk of colon cancer by almost 40% compared to diets that were low in fiber (8). Other studies have confirmed this association as well but the biological mechanism for this association is still unclear (8).

7. Obesity

Over the past 30 years the rates of obesity have increased dramatically. The prevalence actually doubled among adults aged 20 years and older between the years 1980 and 2002 (20). A

more recent study of the prevalence of obesity in the United States analyzed data from the National Health and Nutrition Examination Survey (NHANES) from 2003 to 2004. The researchers used body mass index (BMI), the ratio of weight in kilograms to the square of height in meters, in order to calculate rates of overweight and obesity. The World Health Organization has set forth a standard definition of each weight class based on BMI (Table 1, below). The results of the study showed that based on these definitions, in 2003-2004, 61.8% of adult women were considered overweight or obese. The prevalence of obesity (BMI of greater than 30 kg/m2) was 33.2% and extreme obesity (BMI of greater than 40 kg/m2) was 6.9%. Non-Hispanic black women had the highest prevalence for all categories: overweight or obese, obese, and extremely obese at 81.6%, 53.9%, and 14.7% respectively (21). These rates are alarming considering the increased risk of morbidity and mortality associated with a higher BMI (22).

TABLE 1 Definitions of body mass index and waist circumference categories[a]

Determinant	Body mass index (kg/m^2)	
Underweight	<18.5	
Normal weight	18.5–24.9	
Moderately overweight	25.0–29.9	
Overweight	≥25.0	
Preobese	25–29.9	
Obesity	≥30.0	
Obese class I	30–34.9	
Obese class II	35–39.9	
Obese class III	≥40.0	
	Waist circumference	
	Women	Men
Above action level 1	≥80 cm (~32 in)	≥94 cm (~37 in)
Above action level 2	≥88 cm (~35 in)	≥102 cm (~40 in)

[a]Body mass index categories are defined according to the World Health Organization guidelines (92). Waist circumference categories are suggested by Lean et al (46).

A number of studies have shown that being overweight is associated with increased risk of colorectal cancer (7). A case-control study conducted by Caan et al. found that men who had a BMI in the highest quintile were almost 2 times as likely to develop colon cancer as men with a

BMI in the lowest quintile (OR = 1.96; 95% CI 1.50 – 2.57). Women with a BMI in the highest quintile were about 1.5 times as likely to develop colon cancer when compared to women with BMIs in the lowest quintile (OR = 1.45; 95% CI 1.08 – 1.94). The study also found that these associations were much stronger among younger men and women with a family history of colon cancer (17). Another study looking the association between BMI and colon cancer risk found that those with a BMI >= 30.0 kg/m^2 had an increased risk of developing colon cancer compared to those with a normal BMI (OR = 1.54; 95% CI 1.03 – 2.31). The study also found that those whose BMI increased by more than 10 kg/m^2 between their 30s and the time of recruitment into the study had a higher risk of developing colon cancer than those whose BMI did not change as much (18). Obesity is an important risk fact to consider based on the recent trends in the U.S. If there is a strong association between BMI and colon cancer risk, then continually increasing obesity rates will only increase the incidence of colon cancer throughout the population.

8. Physical Activity

Studies have also found that physical activity is associated with lower risk of colorectal cancer. A meta-analysis published in 2004 found that among 47 studies that examined the association between colon and/or colorectal cancer and physical activity, physically active males had a lower risk of developing colon cancer regardless of specific type of activity (recreational or occupational) and regardless of the type of study (cohort or case-control) (9). The study found that women who participated in recreational physical activity also had a lower risk of developing colon cancer in both cohort and case-control studies but that occupational physical activity among women only showed a reduced risk for colon cancer among case-control studies. Additionally, this meta-analysis found no association between physical activity and risk of rectal

cancer. Another study examined physical activity based on data from the European Prospective Investigation into Cancer and Nutrition (EPIC) (10). A test for heterogeneity found no statistically significant difference in the results for men and women for overall physical activity and each type of physical activity (occupational, household, and recreational) in their association with colon and rectal cancers. Further analysis showed that physically active adults were at a reduced risk for colon cancer compared to inactive adults (RR = 0.78; 95% CI 0.59 – 1.03) with recreational activity being the most protective form of physical activity. This study also found that increased physical activity was not associated with a reduction in rectal cancer risk. While this study showed no difference in the association between physical activity and colon cancer risk among men and women, other studies have found that physical activity is not associated or only modestly associated with reduced risk of colon cancer in women (11, 12). The conflicting results of these studies are evidence that further research is needed to determine the true associations between physical activity and colon cancer risk.

One aspect of physical activity that has not been considered in the majority of the studies looking at physical activity and colorectal cancer risk is lifetime change in physical activity. A case-control study conducted at the German Cancer Research Center collected data about recreational and occupational physical activity at ages 20, 30, 40, 50, and 60 years for each subject. The results of the study showed that the odds ratio was 0.26 (95% CI 0.08 – 0.84) for colon cancer risk for lifelong constantly high-exercisers compared with lifelong non-exercisers (13). This study found no association between lifetime physical activity and risk of rectal cancer. Further analysis of lifetime physical activity patterns including type, frequency, and duration will strengthen our understanding of the potential association between physical activity and colon cancer risk.

Screening Tests

Currently there are a number of different types of screening tests that are offered that test for colon cancer. If benign polyps can be caught early and removed, someone will be much less likely to develop cancerous tumors. The first type of test is the fecal occult blood test (FOBT). The FOBT tests for blood in the stool which may be a sign that there are large polyps in the colon. The test is usually given to a patient to conduct themselves at home. Samples of stool are taken from three separate bowel movements and returned to the lab for examination. If blood is found, a colonoscopy is recommended. It is suggested that this test be conducted annually for those over the age of 50 and earlier for those who have a family history of colon cancer (23). Regular use of the fecal occult blood test can "reduce the risk of death from colorectal cancer by 15% - 33%" (2). Early detection of large polyps in the colon through FOBT screening can also decrease the incidence of colorectal cancer by approximately 20% (2).

The next type of screening test is called a flexible sigmoidoscopy. This is when a doctor or other member of a trained medical staff uses a flexible, lighted tube to examine the lower part of the colon as well as the rectum. The tube, also called a sigmoidoscope, "is about 2 feet long (60 cm) and can visualize clearly about one-third of the colon" (2). If the doctor finds polyps during this test he/she will remove them and collect other tissue samples as well (23). The doctor may even recommend follow-up with a colonoscopy. For cancers within that lower portion of the colon, a flexible sigmoidoscopy test can reduce the risk of death from colorectal cancer by approximately 60% (2). The CDC recommends that the sigmoidoscopy is conducted every 5 years and also recommends use of the sigmoidoscopy in conjuction with an annual FOBT (23).

A colonoscopy is also an effective screening tool for colon cancer. This test is like the

sigmoidoscopy but the instrument that is used is much longer and allows the doctor to examine the inside of the entire colon. For both the sigmoidoscopy and the colonoscopy, the patient usually takes some for of laxatives the day before the test to clean out the colon and rectum for examination. During a colonoscopy, the doctor may remove polyps by using a long wire instrument. According to the National Polyp Study, undergoing colonoscopies on a regular basis can prevent anywhere from 76% to 90% of all colon cancers (2). It is recommended, for people over 50, that colonoscopies be conducted every 10 years (23) and when needed as a follow-up due to results of one of the other screening tests. There are additional screening tests that may be used (barium enema or digital rectal exam) but despite the fact that all of these effective screening tests exist for colorectal cancer it remains one of the leading causes of cancer deaths in the United States.

Improving Prevention

One of the biggest steps that must be taken in order to prevent colorectal cancer is to increase screening. In 2000, approximately 60% of the U.S. population over 50 years of age had not received a colon endoscopy within the last 5 years or a FOBT within the previous year (3). This is a major public health concern considering the fact that early detection could prevent up to 90% of all colorectal cancer cases. A number of things can be done to increase screening rates across the country. First, at-risk populations must be educated. This education may occur through primary physicians, local hospitals, and/or national media campaigns. The CDC has developed a comprehensive educational program called “Screen for Life: National Colorectal Cancer Action Campaign” with spokespeople like Jimmy Smits, Diane Keaton, and Katie Couric. The campaign was developed early in 1999 and continues to foster educational

initiatives today. PSAs, pamphlets, brochures, and fact sheets are all part of the campaign and can be viewed at http://www.cdc.gov/cancer/colorectal/sfl/.

In addition to its national campaign, the CDC is also trying to increase screening efforts through a colorectal cancer screening demonstration program that is currently being offered in 5 sites: Baltimore, MD; St. Louis, MO; the state of Nebraska; Suffolk County, NY; and Seattle, WA. These sites offer free colorectal screenings and follow-up to low-income men and women over the age of 50 (24). More information about these programs can be found at http://www.cdc.gov/cancer/colorectal /what_cdc_is_doing/demonstration/. Other barriers besides lack of education or access to care must also be addressed in order to reduce the incidence and death rates of colorectal cancer. These barriers include failed doctor-to-patient communication, lack of insurance coverage of screening tests, and participants being too busy, embarrassed, or uncomfortable to undergo the different types of screening (2). In order to improve the doctors' communications with their patients, comprehensive organizational changes must be implemented. This may include provider workshops or electronic reminders that will help physicians offer these services to their patients. A physician must also be knowledgeable enough to convince his/her patient that screening is well worth it in the long run: that it may actually save that patient's life. Policy can also play a very important role in ensuring that at-risk populations can access screening tests on a regular basis. Legislation has already been passed in 16 states and the District of Columbia mandating that private insurance companies add colon cancer screening tests to their list of coverages (2). Medicare has also changed its policy in the last decade to include coverage of screening tests as well (2).

Not only can increased screening improve prevention, but changes in personal behaviors can also help to reduce the rates of colon cancer in our country. Changes in dietary patterns,

increasing physical activity, staying at a healthy weight, and reducing one's exposure to harmful tobacco smoke can all reduce one's risk of developing colon cancer. Individual changes along with nation-wide, comprehensive changes in education, organization, and policy will allow us to reach the goals outlined in Healthy People 2010 by the Center for Disease Control and Prevention and the National Institutes of Health to further reduce the number of deaths associated with colon cancer.

Helpful Websites

Center for Disease Control and Prevention

http://www.cdc.gov/cancer/colorectal/

National Cancer Institute

http://www.cancer.gov/cancertopics/types/colon-and-rectal

National Cancer Institute: List of Cancer Centers by State

http://cancercenters.cancer.gov/cancer_centers/cancer-centers-list.html

SEER: Surveillance Epidemiology and End Results

http://seer.cancer.gov/

Guide to Increasing Colon Cancer Screening Rates

http://www.nccrt.org/documents/general/increasecolorectalcancerscreeningrates.pdf

Screening Facts

http://www.cdc.gov/cancer/colorectal/pdf/fs-patient.pdf

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