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AN OVERVIEW OF COLORECTAL CANCER, RISK FACTORS AND EARLY DETECTION

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Abstract:

Colorectal cancer (CRC) is an extremely frequent and fatal disease. The risk of developing CRC is influenced by both environmental and genetic variables, which are covered in this article. The epidemiology of CRC and colorectal screening, as well as the benefits and drawbacks of colonoscopy, are all highlighted. We conducted a narrative review analysis utilizing a comprehensive literature search in MEDLINE/PubMed (using combinations of the following search terms: " colorectal cancer, Colonoscopy, diagnosis, screening, risk factors" " our search was completed in June, 2019. Regular screening can help avoid a variety of colorectal cancers. Screening can detect precancerous polyps, which are abnormal growths in the colon or rectum that can be removed before they develop into cancer. Colorectal cancer is highly treatable when detected early, thus screening is crucial. Colorectal cancer has no symptoms in the early stages, but they arise as the cancer grows. According to the American Cancer Society, colorectal cancer screening should begin around the age of 45. A colonoscopy is the most effective colorectal cancer screening test available. It is the only test that can also prevent a variety of colorectal cancers.

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INTRODUCTION:

Incidence and mortality rates of colorectal cancer (CRC) vary widely throughout the world. According to the GLOBOCAN data source of the World Health Organization, CRC is the third most often diagnosed cancer in men and the second in women worldwide, with approximately 1.8 million new cases and 861,000 deaths in 2018 [1]. Men have rates significantly greater than women.

Colorectal cancer is a slow-growing disease that begins with a tumor or tissue growth on the inner lining of the rectum or colon [2]. If this rare growth, known as a polyp, becomes cancerous, it can form a tumor on the wall of the rectum or colon and then spread into blood arteries or lymph vessels, increasing the likelihood of metastasis to other physiological areas [2]. The overwhelming majority (over 95%) of colorectal cancer cells are adenocarcinomas [2]. These begin in the glands that produce mucus that line the colon and rectum [2], [3]. Other less frequent cancers of the colorectal region include carcinoid tumors (which begin in hormone-producing intestinal cells), intestinal stromal tumors (which form in specialized colonic cells known as interstitial cells of Cajal), lymphomas (immune system cancer cells that form in the colon or rectum), and sarcomas (which typically begin in blood vessels but occasionally form in colorectal wall surfaces) [2], [3].

In the 1960s, Drs. William Wolff and Hiromi Shinya devised a method for penetrating the entire length of the colon with an electronic sensor-equipped tube [4]. Since its beginnings, colonoscopy has become a common method for detecting colorectal cancer and treating a number of disorders of the lower digestive tract.

METHODOLOGY:

Comprehensive literature search was performed in MEDLINE/PubMed and Cochrane Central Register of Controlled Trials (using combinations of the following search terms: " colorectal cancer, Colonoscopy, diagnosis, screening, risk factors" " our search was concluded on June, 2022. Extracted data from individual studies were summarized according to the main objects that our study is concerned about: Colorectal screening, a method for detecting colorectal cancer.

DISCUSSION:

Epidemiology:

Colorectal cancer is the third most prevalent cancer in men and the second most prevalent cancer in women. In 2018, there were over 1,8 million new instances [1]. The tables below [1] list the top 25 countries with the highest rates of colorectal cancer in 2018.

Table 1. Colorectal cancer rates: both sexes [1].

Rank	Country	Age-standardised rate per 100,000
1	Hungary	51.2
2	South Korea	44.5
3	Slovakia	43.8
4	Norway	42.9
5	Slovenia	41.1
6	Denmark	41.0
6	Portugal	40.0
8=	Barbados	38.9
8=	Japan	38.9
10	Netherlands	37.8
11	Australia	36.9
12	Singapore	36.8
13	Serbia	36.7
14=	Belgium	35.3
14=	New Zealand	35.3
16=	Uruguay	35.0
16=	Brunei	35.0
18	Moldova	34.2
19	Croatia	34.1
20	Ireland	34.0
21	Spain	33.4
22	Latvia	33.0

23	Czech Republic	32.7
24	UK	32.1
25	Belarus	31.8

Risk Factors for CRC:

Age, genetic and environmental factors play a significant role in the progression of colorectal cancer. Lynch Syndrome (Hereditary nonpolyposis colorectal cancer), Familial adenomatous polyposis (FAP), and MUTYH-associated polyposis are hereditary colorectal cancer illnesses (MAP). Lynch syndrome and Familial adenomatous polyposis account for the great majority of hereditary colorectal cancer syndromes, which account for around 5% of all colorectal cancer cases [5]. Even in the absence of the preceding hereditary colon cancer syndromes, the existence of a family history of colon cancer in first-degree relatives increases the risk of colorectal cancer in around 20% of cases. With a history of colorectal cancer in first-degree relatives, the risk increases by approximately twofold compared to the general population.

Other notable groups associated with colorectal cancer include African-American race and male gender. Inflammatory Bowel Disease - Ulcerative colitis more often than Crohn's disease, Obesity, sedentary way of life, red meat and processed meat, cigarette use, alcohol use, history of abdominal radiation, acromegaly, renal transplant with use of immunosuppressive medications, Diabetes mellitus and insulin resistance, androgen deprivation therapy, cholecystectomy, coronary artery disease, and ureterocolic ana

Physical activity on a regular basis, a diet rich in fruits and vegetables, a high-fiber diet, a diet rich in folate, calcium, dairy products, vitamin D, vitamin B6, magnesium consumption, fish consumption, garlic, regular use of aspirin and nonsteroidal anti-inflammatory drugs are protective factors associated with a decline in the incidence of colorectal cancer (NSAIDS).

Numerous studies have demonstrated a link between alcohol consumption and the development of colorectal cancer. A meta-analysis of prospective studies demonstrated a slight positive link between heavy alcohol consumption (> 50 g/day) and colorectal cancer mortality [12]. This link was stronger in the Asian population than in the white population, most likely due to genetic factors such as alcohol metabolism, dietary factors such as folate intake, and body composition. The link between alcohol consumption and mortality risk from colorectal cancer was equivalent at several anatomic locations, including the colon and rectum. A potential investigation of Carriers of Mismatch repair deficiency also found a positive relationship between alcohol use (> 28 g/day or 2 drinks per day) with colon cancer [13]. It has been suggested that acetaldehyde, a byproduct of ethanol, causes cancer through affecting DNA synthesis, repair, the structure and function of glutathione, and the proliferation of colonic mucosa.

Numerous observational studies have found a relationship between obesity and colon cancer risk (20-30% per 5 kg/m2 rise in men and 10% per 5 kg/m2 increase in women) [17]. A Mendelian Randomization Study [17] revealed a stronger connection between obesity and colorectal cancer in women than in males.

Early detection and prevention:

Typically, colorectal cancer develops gradually over several years. If adenomas are discovered and destroyed prior to the progression of cancer, the disease can be averted. In addition, colorectal cancer is largely curable if detected at an early stage. In contrast to the majority of other malignancies, therefore, screening and early detection are exceptional approaches for the secondary prevention of colorectal cancer and related mortality.

Evaluation for colorectal cancer comprises screening for precancerous colon polyps or early-stage cancer before the onset of symptoms, before the disease has a chance to spread, and while treatment is simpler, less expensive, and more likely to be effective [18]. The Centers for Disease Control and Prevention (CDC) and the U.S. Preventive Services Task Force recommend that men and women between the ages of 50 and 75 undergo colorectal cancer screening with high-sensitivity fecal occult blood testing (FOBT), sigmoidoscopy, or colonoscopy [18].

In the general population, stomach symptoms account for up to 10% of general practitioner consultations [19]. Numerous of these symptoms are associated with chronic functional disorders (irritable bowel syndrome, chronic constipation) or anorectal benign lesions that do not benefit from colonoscopy screening [19]. In clinical practice, it is common to do a colonoscopy on patients with gastrointestinal symptoms who are suspected of having CRC [19]. In fact, many technique guidelines imply that colonoscopy should be performed for gastrointestinal

symptoms, however the significance and efficacy of symptoms as indicators of CRC are uncertain. While some studies suggest that symptoms and indicators may be effective in diagnosing colorectal cancer, others have found no such link [20]. In addition, few of these studies are recent, and the perception of symptoms may have changed since the earliest studies were conducted.

A Randomization Study [17] revealed a stronger relationship between obesity and colorectal cancer in women than in males.

Benefits of Colonoscopy in early screening:

Many primary colorectal malignancies in persons without inflammatory bowel disease are likely to originate from precancerous polyps [21]. The bulk of these polyps develop by a well-explained chain of mutations over the period of years or even decades. Years ago, it was believed that 25% of men and 15% of women will develop adenomatous polyps by the time they reach the age of 50. Recent research investigations conducted in both academic and community settings indicate that the actual rate may be higher [21]. In addition, the vast majority of these polyps and even very early tumors are symptomless. Since colonoscopy permits the detection and removal of these polyps prior to their transformation into cancer, it would appear to be a perfect screening method. Before colonoscopy could be considered a valid (and valuable) screening method, however, a number of crucial issues needed to be solved. It must be applicable to other available testing modalities as an example. It must be contrasted to flexible sigmoidoscopy (FS), a far less invasive screening technique that does not require sedation and has been found to reduce colorectal cancer incidence and mortality [22]. Several studies examine the safety and efficacy of colonoscopy as a primary screening test for asymptomatic individuals. Lieberman and his colleagues released the VA Cooperative Study-380 in 2000 [23]. This research associate investigated 3196 patients, of whom 3121 underwent a full colonoscopy. Patients with adenomas in the distal colon were significantly more likely to develop adenomas in the proximal colon than those without such lesions; nevertheless, 52 percent of individuals with novel proximal neoplasia did not have distal adenomas. Consequently, advanced proximal lesions would have been overlooked in almost fifty percent of patients in an FS-based evaluation program. The fact that over 97 percent of the participants were male is a significant limitation of this study. Concern was undertaken to determine the efficacy of primary screening colonoscopy in asymptomatic females by Schoenfeld and colleagues [24]. Only 35% of females with proximal neoplasia who underwent full colonoscopy would have had their lesions detected by flexible sigmoidoscopy, according to this prospective associate study of 1,463 women. The authors concluded that colonoscopy may be the most effective CRC screening method for females. Colonoscopy detects more adenomas than flexible sigmoidoscopy, according to this research. Possibly of even greater concern is the impact of adenoma removal (polypectomy) on the incidence and death of colorectal cancer.

Benefit of Colonoscopy on Colon Cancer Incidence and mortality:

There is credible evidence that colonoscopy plus polypectomy reduces the risk of colorectal cancer in individuals. The National Polyp Study, which was published in 1993 [25], was the first study to suggest this advantage. Despite significant limitations, such as the use of historical controls, this study concluded that colonoscopic polypectomy may prevent between 76 and 90 percent of colorectal cancer cells. Comparable studies conducted in Italy by Citarda and colleagues indicated a 66% reduction in the incidence of colon cancer [26]. Again, this study was limited in that controls were not drawn from a matched cohort; rather, a mathematical model was used to predict the expected CRC incidence in a hypothetical population.

As with all other outcomes of colonoscopy screening, the evidence supporting a decrease in CRC mortality is indirect. Nonetheless, the consistency of the data convinces us that colonoscopy screening provides a substantial benefit, even though the extent of this benefit is not precisely defined. Two primary study approaches have thus far been employed to investigate this question: retrospective case-control studies and prospective cohort studies. While neither technique has the strength of a randomized controlled trial, the majority of research authors have worked diligently to strengthen the analytical limitations inherent to the studies' designs, and these research studies represent the best available science upon which clinicians must base decisions regarding patient care. Table 4 contains these investigations [27-30].

In 2009, Baxter and colleagues published a population-based, case-control study examining people who were diagnosed with CRC between 1996 and 2001 and who died of CRC by 2003. Each case was paired 1:5 with a control. The scientists saw a remarkable 67% decrease in colorectal cancer on the left side, but none on the right. There are a number of important restrictions to keep in mind with this study.

The cecal intubation rate of 79-83% is much lower than the projected rates of 95% for screening exams and 90% for all evaluations [31]. While the authors adequately controlled for this by doing a sub-analysis on "full" colonoscopies, the low rate of cecal intubation may reflect poor colonoscopy technique (including evaluation for adenomas) that such modifications will not ameliorate. The reduced polyp detection rate of 26% among case patients provides additional support for this idea. Existing standards include a 25% adenoma detection rate in men and a 15% adenoma detection rate in women [32]. Given that a number of the polyps discovered in the study were probably hyperplastic, one would anticipate a total polyp detection rate (adenomas + hyperplastic) in the 30-40% range. A further limitation is the fact that not all colonoscopies included were conducted for screening purposes. Patients with symptomatic cancer cells that provoked the examination would be cases based on the design, but they would have a greater likelihood of having advanced disease and hence a lower chance of benefiting from the screening test. Despite these limitations, the difference between right and left sided advantage in this study is remarkable and should not be taken lightly.

Singh et al. identified a comparable distinction in the colonoscopy's safety advantage. In his retrospective cohort analysis, Singh utilized Manitoba's claims database to compare the CRC mortality rate of patients who had colonoscopic CRC screening to the CRC mortality rate of the general population. In evaluating 54,803 patients, he took note of a 29% overall decline in CRC mortality, which was entirely attributable to a decline in left-sided cancer deaths. Remarkably, when the authors stratified the data by the speciality of the endoscopists, gastroenterologists were associated with a 59% reduction in right-sided CRC. This strongly suggests that the type of examiner (and, by extension, his or her training and experience) plays a significant role in optimizing the efficiency of colonoscopy as a CRC screening technique.

Rabeneck and colleagues conducted a cohort study on all 50-90-year-old Ontario residents on January 1, 1993, in which they followed patients for 14 years and stratified them according to the "intensity of colonoscopy usage" in their region. They adjusted for age, gender, comorbidity, income, and residence using multivariable analysis (city vs. rural). Rabeneck discovered that the risk of death fell by 3% for every 1% increase in the complete colonoscopy rate. While there are various limitations to this research study, including the inability to attribute causality, the significance of the result, the size of the sample research study, and the biological plausibility of the search provide fuel for thought.

National Polyp research conducted one of the most recent studies addressing the impact of colonoscopy screening on CRC mortality. The scientists analyzed 2602 patients who had undergone colonoscopic polypectomy to remove adenomas and were then followed for a mean of 15.8 years. Compared to historical controls, this group experienced a 53% decrease in CRC. Despite the fact that this study is limited by the fact that endoscopies were only performed in specialized centers, the results are persuasive, especially since they are consistent with other studies in demonstrating a clear reduction in mortality associated with testing.

CONCLUSION:

Colon cancer is a fatal disease that affects and kills many, many people worldwide, primarily in the West; but, due to Western influences, colorectal cancer is on the rise in many Eastern countries as well. According to research, certain dietary factors, namely high meat and animal-fat consumption, can increase colorectal carcinogenesis, but other nutritional factors, such as fish, fiber, vitamin D, and calcium, can help prevent it. In addition, research has established a hereditary link to colorectal cancer, finding that around 35% of risk is due to genes and demonstrating how heredity can present both risks and preventive effects. In addition, both genetic and environmental factors influence the risk of colorectal cancer. Intestinal cancer prevention and/or treatment can be challenging. As previously stated, regular eating of fish, fiber, vitamin D, and calcium, as well as regular exercise and aspirin, can help prevent the development of colorectal cancer. Numerous colorectal cancers can be avoided with routine screening. Screening can detect precancerous polyps, which are abnormal growths in the colon or rectum, so they can be removed before they develop into cancer. Screening is essential because colorectal cancer is highly curable if detected early. Early stages of colorectal cancer typically lack symptoms, which tend to manifest as the disease advances. The American Cancer Society proposes that screening for colorectal cancer should begin at age 45. Colonoscopy is the most effective screening method for colorectal cancer. It is the only screening test capable of preventing many colorectal cancers.

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