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Research Article

ROLES OF COLONOSCOPY IN EARLY DETECTION OF COLORECTAL CANCER AND REVIEWING RISK FACTORS

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Abstract:

Colorectal cancer (CRC) is a common and lethal disease. The danger of obtaining CRC is affected by both ecological and genetic factors, which are discussed in this review. The epidemiology of CRC and Colorectal screening, pros and effect of Colonoscopy are emphasized as well. We conducted a narrative review study that performed through Comprehensive literature search was performed in MEDLINE/PubMed (using combinations of the following search terms: " colorectal cancer, Colonoscopy, diagnosis, screening, risk factors" " our search was ended on June, 2019. Numerous colorectal cancers can be prevented with regular testing. Screening can locate precancerous polyps-abnormal growths in the colon or rectum- to make sure that they can be eliminated before they turn into cancer. Screening is critical since when found early, colorectal cancer is highly treatable. Early stages of colorectal cancer generally existing no symptoms, which tend to appear as the cancer progresses. The American Cancer Society suggests that colorectal cancer testing ought to start at age 45. A colonoscopy is the best screening test available for colorectal cancer. It is the only testing test that also can prevent numerous colorectal cancer

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INTRODUCTION:

Colorectal cancer (CRC) incidence and death rates vary markedly worldwide. Around the world, CRC is the third most frequently detected cancer in males and the 2nd in women, with 1.8 million new instances and practically 861,000 deaths in 2018 according to the World Health Organization GLOBOCAN data source [1]. Rates are significantly greater in men than in females.

The term colorectal cancer describes a slowly developing cancer that starts as a tumor or tissue growth on the internal lining of the rectum or colon [2]. If this uncommon growth, referred to as a polyp, eventually comes to be cancerous, it can create a tumor on the wall of the rectum or colon, and subsequently grow into blood vessels or lymph vessels, raising the opportunity of metastasis to various other physiological sites [2]. Of the cancers cells that begin in the colorectal area, the huge majority (over 95%) are identified as adenocarcinomas [2]. These begin in the mucus-making glands lining the colon and rectum [2], [3]. Other less-common cancers of the colorectal region include carcinoid tumors (which commence in hormone-producing intestinal cells), intestinal stromal tumors (which create in specialized colonic cells known as interstitial cells of Cajal), lymphomas (immune system cancers cells that develop in the colon or rectum), and sarcomas (which commonly begin in blood vessels but occasionally type in colorectal wall surfaces) [2], [3].

In the 1960s, Drs. William Wolff and Hiromi Shinya established a way to penetrate the full length of the

colon using a tube with electronic sensors [4]. Given that its inception, colonoscopy has ended up being a popular approach for testing of colorectal cancers and for dealing with a variety of conditions of the reduced stomach tract.

Colorectal cancer (CRC) is a common and lethal disease. The danger of obtaining CRC is affected by both ecological and genetic factors, which are discussed in this review. The epidemiology of CRC and Colorectal screening, pros and effect of Colonoscopy are emphasized as well.

METHODOLOGY:

We conducted a narrative review study that performed through 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 ended on June, 2019. Extracted data from individual studies were summarized according to the main objects that our study is concerning about Colorectal screening, and effect of Colonoscopy.

DISCUSSION:

Epidemiology: Colorectal cancer is the 3rd most commonly occurring cancer in men and the 2nd most commonly occurring cancer in women. There were more than 1.8 million new instances in 2018 [1]. The top 25 countries with the highest rates of colorectal cancer in 2018 are given in the tables listed below [1].

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: Age, genetic and environmental points play a major function in the advancement of colorectal cancer. Hereditary colorectal cancer disorders consist of Lynch Syndrome (Hereditary nonpolyposis colorectal cancer), Familial adenomatous polyposis (FAP), MUTYH-associated polyposis (MAP). Lynch syndrome and Familial adenomatous polyposis contribute to a vast bulk of hereditary colorectal cancer syndrome, which represent just roughly 5% of entire colorectal cancer incidence ^[5]. The presence of family history of colon cancer in first degree relatives, even in the lack of the above hereditary colon cancer syndromes, raise the risk of growth of colorectal cancer in around 20% of instances. The risk increases over twofold, when compared to the general populace,

with a history of colorectal cancer in first degree relatives.

Other well-known organizations with colorectal cancer include African American ethnicity, male sex, Inflammatory Bowel ailment - Ulcerative colitis more frequently than Crohn's disorder, Obesity, sedentary way of living, red meat (Table 2) 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 treatment, cholecystectomy, coronary artery disorder and ureterocolic anastomosis ^[5].

Table 2. Summary of major epidemiological studies examining the association of Red Meat Intake with CRC.

Author, Year	Study Design	Country/Center	Result
Chao A, 2005 [6]	Observational	USA	Positive association—long term meat consumption increased the risk of cancer in the distal portion of the large intestine
Norat A, 2005 [7]	Case-Control	10 European Countries	Positive association—high intake (>160 g/day) group had a risk 1.35-fold as compared with the lowest intake (<20 g/day)
Willett WC, 1990 [8]	Observational	USA	Positive association - RR of CRC in women who ate beef, pork or lamb as a main dish every day was 2.49, as compared with those reporting consumptions less than once a month.
Cross AJ, 2010 [9]	Observational	USA	Positive association—heme iron, nitrite, heterocyclic amines from meat may explain these associations
Chan DS, 2011 [10]	Meta-analysis of ten cohort studies	N/A	Positive association—17% increased risk per 100 g per day of red meat and an 18% increase per 50 g per day of processed meat
Beresford SA, 2006 [11]	Randomized controlled trial	USA	No association—a low-fat dietary pattern intervention did not reduce the risk of colorectal cancer in postmenopausal women during 8.1 years of follow-up

Protective factors that have been associated with a decline in the incidence of CRC include routine physical activity, diet rich in fruits and vegetables, high fiber diet regimen, folate rich diet regimen, Calcium, Dairy products, Vitamin D, Vitamin B6, magnesium consumption, fish usage, garlic, regular use Aspirin, Non-Steroidal Anti-Inflammatory Drugs (NSAIDS).

Numerous studies have revealed a causal role in between alcohol intake and occurrence of colorectal cancer (Table 3). Meta-analysis of prospective researches has revealed a modest positive association between hefty alcohol use (> 50 g/day) and mortality connected with colorectal cancer [12]. This association

was more powerful in Asian populace than in the white population, likely as a result of hereditary elements such as alcohol metabolism, nutritional factors such as folate intake and body composition. The association of alcohol drinking and risk of mortality from colorectal cancer was comparable at various anatomic sites, such as colon and rectum. A possible study of Carriers of Mismatch repair deficiency likewise revealed a favorable association with alcohol consumption (> 28 g/day or 2 drinks daily) and colon cancer [13]. It has actually been suggested that acetaldehyde, a metabolite of ethanol, is cancer causing by influencing DNA synthesis, repair, change of framework and function of glutathione and boost in colonic mucosal proliferation.

Table 3. Summary of major epidemiological studies examining the association of Alcohol consumption with CRC.

Author, Year	Study Design	Country/Center	Result
Fedirko, 2011 [14]	Meta-analysis of 27 cohort and 34 case-control studies	USA, Europe, Asia, Australia	Positive—strong evidence for an association between alcohol drinking of >1 drink/day and CRC risk.
Cho E, 2004 [15]	Pooled analysis of 8 cohort studies	North America and Europe	Positive—Increased risk for CRC was limited to persons with an alcohol intake of 30 g/d or greater (approximately >or =2 drinks/d)
Mizoue T, 2008 [16]	Pooled evaluation of 5 cohort studies	Japan	Positive- Increased risk with an alcohol consumption of > or =23 g/day.

Numerous observational researches have revealed an association in between excessive weight and risk of colorectal cancer (20- 30% per 5 kg/m² increase in men and ~ 10% per 5 kg/m² boost in women) ^[17]. A Mendelian Randomization Study showed a more powerful association with weight problems and colorectal cancer in women than in men ^[17].

Screening: Colorectal cancer typically develops gradually over many years. The illness can be prevented if adenomas are detected and eliminated prior to the progress to cancer. Additionally, colorectal cancer is primarily treatable if discovered at early stages. For that reason, in contrast to most of other cancers, screening and early detection are outstanding measures for the secondary prevention of colorectal cancer and associated mortality.

Evaluating for colorectal cancer entails screening for pre-cancerous colorectal polyps or early-stage cancer before the manifestation of signs and symptoms, before the ailment has an opportunity to expand or spread out, and while therapy is easier to take care of, less expensive, and more likely to be successful ^[18]. In the United States, the Centers for Disease Control and Prevention (CDC) and the U.S. Preventive Services Task Force advise that men and women between the ages of 50 and 75 be screened for colorectal cancer with high-sensitivity fecal occult blood testing (FOBT), sigmoidoscopy, or colonoscopy ^[18].

In the basic populace, stomach signs account for up to 10% of consultations with general practitioners ^[19]. A lot of these signs are related to chronic functional conditions (irritable bowel disorder, chronic constipation) or anorectal benign lesions that do not benefit from colonoscopy examination ^[19]. In clinical technique, it prevails to execute a colonoscopy in patients with bowel symptoms as a result of the suspicion of CRC ^[19]. In fact, lots of method standards suggest that colonoscopy should be performed for bowel symptoms, however the relevance and value of signs and symptoms as signs of CRC is not well established. While some reports recommend that signs and symptoms might be useful in identifying CRC, others have found no such association ^[20]. Furthermore, few of these research studies are recent and the perception of signs may have transformed since the very early studies were performed.

Benefits of Colonoscopy for CRC Screening: In patients that do not have inflammatory bowel ailment, a lot of primary colorectal cancers are believed to stem from precancerous polyps ^[21]. The majority of these polyps occur over the course of a years or even more

through a well explained series of mutations. For years, our understanding of adenoma frequency was that 25% of men and 15% of females will certainly have adenomatous polyps by the time they reach age 50. Recent research studies conducted in both academic and community practice setups suggest that the true rate may be greater ^[21]. Furthermore, the substantial bulk of these polyps, and even very early cancers, are asymptomatic. Because colonoscopy allows for the discovery and removal of these polyps before the development to cancer, it would seem to be an ideal screening tool. Several essential concerns required to be addressed, nevertheless, before colonoscopy could be taken into consideration a valid (and valuable) screening tool. As an example, it must transcend to other available testing modalities. It must be compared to adaptable sigmoidoscopy (FS), a much less invasive screening method which does not call for sedation and which had been shown to lower colorectal cancer incidence and death ^[22]. A number of trials attend to the safety and efficiency of colonoscopy as a primary screening test in asymptomatic people. The first was the VA Cooperative Study-380 published by Lieberman and colleagues in 2000 ^[23]. This associate research examined 3196 subjects, 3121 of whom went through a complete colonoscopy. While patients with adenomas in the distal colon were statistically more probable to have adenomas in the proximal colon than those without such lesions, 52 percent of those with innovative proximal neoplasia had no distal adenomas. Therefore, advanced proximal lesions would certainly have been missed out on in more than half the patients in an FS based evaluating program. One considerable limitation of this research study is the reality that nearly 97 percent of the subjects were male. To figure out the efficacy of primary screening colonoscopy in asymptomatic female, Schoenfeld and colleagues conducted the Concern trial ^[24]. This prospective associate research study of 1463 women going through full colonoscopy located that only 35% of females with proximal neoplasia would certainly have had their lesions found by flexible sigmoidoscopy. The authors ended that colonoscopy might be the recommended CRC testing tool for females. From these studies, colonoscopy detects more adenomas than flexible sigmoidoscopy. An even more crucial worry, possibly, is the effect of adenoma elimination (i.e. polypectomy) on colorectal cancer incidence and mortality.

Effect of Colonoscopy on Colon Cancer Incidence:

There are reasonably great data to support a decrease in colorectal cancer in those going through colonoscopy with polypectomy. The very first study to suggest this benefit was the National Polyp Study which was released in 1993 ^[25]. While this research

had some substantial constraints, such making use of historical controls, its conclusion that colonoscopic polypectomy might avoid between seventy-six and ninety percent of colorectal cancers cells. A comparable research study carried out in Italy by Citarda and colleagues revealed a reduction in colon cancer occurrence of sixty-six percent [26]. Once more, this research was restricted in that controls were not extracted from a matched cohort, however rather a mathematical model was made use of to determine the expected CRC incidence in a hypothetical group.

Effect of Colonoscopy on Colon Cancer Mortality:

As for all end results of screening colonoscopy, the proof for a decrease in CRC mortality is indirect.

Nevertheless, the consistency of the information assures us that a significant benefit is derived from colonoscopy screening, even if the magnitude of that advantage is not completely defined. Thus far, 2 primary study designs have been utilized to deal with the question: retrospective case-control studies and potential cohort studies. While neither technique has the strength of a randomized controlled trial, most research writers' have functioned diligently to shore up the analytical restrictions inherent in the studies' designs and these research studies represent the best offered science on which clinicians must base patient care choices. These studies are provided in table 4 [27-30].

Table 4. Major trials addressing a reduction in CRC mortality.

Author	Year	Design	N	CRC Mortality Reduction
Baxter [27]	2009	Case-Control	10,292 (Case) 51,460 (Control)	67% - left sided 1% (NS) -right-sided
Singh [28]	2010	Cohort	54,803	29% overall 47% left-sided 0% right-sided
Rabeneck [29]	2010	Cohort	2,412,077	3% decrease/1% increase in colonoscopy
Zauber [30]	2012	Cohort	2602	53% overall

In 2009, Baxter and colleagues released a population based, case-control study checking out subjects that received a CRC medical diagnosis in between 1996 and 2001 and that died of CRC by 2003. They matched each situation 1:5 with a control. The authors noted an impressive 67% reduction in left sided colorectal cancer but none in right sided illness. This research has a number of vital constraints worth keeping in mind. The cecal intubation rate of 79-83% is considerably below the 95% rate which would be expected for screening examinations and 90% for all assessments [31]. While the authors appropriately regulated for this by performing a sub-analysis on "complete" colonoscopies, the low rate of cecal intubation might mirror general bad colonoscopy method (consisting of assessment for adenomas) which such adjustments will certainly not reduce. Additional assistance for this concept is in the reduced polyp discovery rate of 26% in case patients. Existing requirements determine a 25% adenoma discovery rate in men and a 15% adenoma discovery rate in women [32]. Considered that a variety of the polyps detected in the study were most likely hyperplastic, one would anticipate a complete polyp detection rate (adenomas + hyperplastic) to be in the 30-40% variety. An additional constraint is the truth that not all the colonoscopies included were performed for screening. Patients with symptomatic

cancers cells which prompted the exam would certainly be situations based upon the design, however, would certainly have much more probability of having progressed disorder, and therefore less opportunity of taking advantage of the screening test. Despite these restrictions, the distinction in right and left sided advantage in this research study is impressive and ought to not be gently disregarded.

Singh et al. discovered a similar difference in the safety benefit of colonoscopy. In his retrospective cohort study, Singh made use of Manitoba's claims database to compare CRC mortality between patients that had colonoscopic CRC screening versus the standardized CRC death rate for the general populace. In analyzing 54,803 subjects, he kept in mind a 29% overall decrease in CRC mortality, all of which was stemmed from a decrement in left-sided cancer mortalities. Remarkably, when the authors stratified the data according to the specialty of the endoscopists, gastroenterologist conferred a decrease in right sided CRC of 59%. This strongly recommends that the type of examiner (and by extension their training and experience) matter greatly in maximizing the efficiency qualities of colonoscopy as a CRC screening tool.

Rabeneck and coworkers executed a cohort study on all grownups 50-90 years of ages living in Ontario on 1 January 1993 in which they complied with subjects for 14 years and stratified them by the "intensity of colonoscopy use" in their area. They did multivariable analysis readjusting for age, sex, comorbidity, earnings, and residence (city vs. rural). Rabeneck discovered that for each 1% Increase in the full colonoscopy rate, the risk rate of death decreased by 3%. While there are several constraints to this research study, consisting of a lack of ability to attribute causality, the magnitude of the result, the size of the sample research study, and the biologic plausibility of the searching for offer food for thought.

One of the most current research studies to attend to the result of screening colonoscopy on CRC death was from the National Polyp research. The authors examined 2602 patient that had had adenomas removed via colonoscopic polypectomy and after that were complied with for a mean of 15.8 years. Contrasted to historic controls, this group took pleasure in a 53% reduction in CRC. While this research study is restricted by the truth that endoscopists were done in expert centers, the results are nonetheless compelling, particularly since they are in keeping with prior research studies in revealing a clear reduction in mortality in association with testing.

CONCLUSION:

Colorectal cancer is a lethal ailment that affects and eliminates numerous, lots of people across the planet, mainly in the West; nonetheless, as a result of Western influences, colorectal cancer is on the rise in lots of Eastern countries too. Research study informs us that some dietary variables, specifically high meat and animal-fat intake, can promote colorectal carcinogenesis, whereas various other nutritional aspects, such as fish, fiber, vitamin D, and calcium, can help avoid it. Research has additionally elucidated a hereditary link to colorectal cancer, describing that roughly 35% of risk is because of genes, and revealing how genetics can provide both threats and protective effects. On top of that, hereditary elements and environmental elements jointly affect the risk of colorectal cancer.

The avoidance and/or control of intestines cancer can be complex. As formerly pointed out, the normal intake of fish, fiber, vitamin D, and calcium, in addition to routine workout and aspirin consumption, can all aid avoid the growth of colorectal cancer.

Numerous colorectal cancers can be prevented with regular testing. Screening can locate precancerous

polyps- abnormal growths in the colon or rectum- to make sure that they can be eliminated before they turn into cancer. Screening is critical since when found early, colorectal cancer is highly treatable. Early stages of colorectal cancer generally existing no symptoms, which tend to appear as the cancer progresses. The American Cancer Society suggests that colorectal cancer testing ought to start at age 45. A colonoscopy is the best screening test available for colorectal cancer. It is the only testing test that also can prevent numerous colorectal cancers.

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