ANALYSIS OF IMPACT OF COLORECTAL CANCER IN WOMEN

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ABSTRACT: Smoking is a newly identified risk factor for cancer of the colon. We decided to discuss the possibility that women could be more vulnerable to smoking-related colon cancer than men as one of the potential reasons for the elevated risk of colon cancer. We tracked 68,160 women aged 30–69 from the Norwegian Women and Cancer Survey who completed a questionnaire in 1996 or 1998 by connecting to national registries until 31 December 2005. Rate ratios (RRs) and 95 % confidence intervals (CIs) were calculated by fitting Cox proportional hazard models. Subsequently, we measured the population due to the percentage. Throughout the normal 14-year follow-up, 2,333 Norwegian males and females died of CRC (60 percent males). Ever smokers of males and females had a 20 percent (HR 1.23, CI 1.08–1.40 and HR 1.22, 95 percent CI 1.06–1.40, respectively) decreased risk of death from CRC relative to non-smokers of the sex. Women ever smokers had a 50 per cent (HR 1.49, 95 per cent CI 1.20–1.87) increased risk compared to women never smokers for proximal colon cancer mortality. The elevated risk of death from rectal cancer for male smoking was around 40 per cent higher (HR 1.43, 95 per cent CI 1.14–1.81) relative to male smokers never smokers.

1. INTRODUCTION

In its monograph on cigarette smoke and cancer risk published in 2004 [1], the International Agency for Research on Cancer concluded that there was not enough data to identify smoking as a causal factor for colorectal cancer. However, the consensus in the most recent monograph on this subject released in 2012 [2] was that the association between smoking and colorectal cancer may be causal. Globally, the third and second most prevalent cancer in men and women is colorectal cancer (CRC), respectively. Incidence rates differ but men have higher rates than women in all the 15 countries with the highest incidence rates. Over the last 50 years this has also been the case in Norway. While Norwegian men rank 13 among countries for their levels of occurrence of colon cancer, Norwegian women rank number two. CRC occurrence in Norway is 43 for men and 35 for women per 100,000 person-years, when age-adjusted to the regular world population [3]. Mostly this difference is attributed to men with significantly more rectal but not more colon cancer than women. In the late 50s, for both men and women, the prevalence rate for colon cancer was 10 per 100,000 person-years, which rose in the same manner until 1980. From 1954 until 2008, colon cancer prevalence rates for both men (up to 26.2 per 100,000 person-years) and women have more than doubled.

There is no known link between cigarette smoking and colorectal cancer (CRC). In Norway, with a total of 1,767 incidence cases among women in 2006, CRC is the second most prevalent cancer identified after prostate cancer among men and breast cancer among females [1]. The age-adjusted prevalence rate of CRC has been doubled for all sex in the past 50 years. In 2002, Norwegian women had the world's second-highest incidence of CRC, exceeded only by New Zealand women [2]. Thus far, there has been no clear reason for Norwegian women's rising danger and top ranking [3]. Worldwide CRC is one of the most common, high-mortality cancers [2]. Giovannucci et al [4] proposed in 1996 that smoking was an initiator of colorectal carcinogenesis, but that the elevated incidence occurred just 30–40 years after the initiation of smoking. One has accepted the idea that smoking is a risk factor for CRC [5]. Nonetheless, two 2004 studies, one from the International Cancer Research Agency [6] and the other from the US Surgeon General [7], noted that there was insufficient evidence to suggest that the association between smoking and CRC is causal. Since tobacco use amongst women is may globally [8, 9] smoking will lead to large numbers of CRCs if a causal relationship exists

The rate of smoking in Norway among men in 1973 was around 52%; by 2007 there was a drop of over 50% to 24%. Between 1973 to 2002 the percentage of female smokers stood at about 30 percent. There was a significant decrease in women who smoked on a daily basis after 2002, and by 2007 the rate of women smokers was close to that of men [9–11]. We also previously stated that there could be greater chance of colon cancer due to cigarette smoking in women than in men [12]. The key aim of this research was to prospectively investigate the relationship between cigarette smoking in a large Norwegian population and CRC mortality. We also decided to inquire how gender varied in the group.

2. Researcher's views

Carmen Lilla et al., 2006 [13] examined the impact of variations in acetylation ability, determined by genotypes NAT1 and NAT2, on the risk of colorectal cancer associated with exposure to cigarette smoke or the intake of red meat. 505 patients with incident colorectal cancer and 604 age- and sex-matched control individuals with genotyping data and detailed information about risk factor were included in this population based case-control study in Germany. The genotyping of NAT1 and NAT2 genetic polymorphisms was performed using a melting curve analysis approach based on fluorescence. Using multivariate logistic regression the relationship between genotypes, environmental factors, and colorectal cancer risk was measured. Colorectal cancer risk associated with active smoking was raised after 30 + packyears of smoking duration [odds ratio (OR), 1.4; 95 per cent confidence interval (95 per cent CI), 0.9-2.2] but not

substantially altered by either NAT1 or NAT2 genotype. Outdoor cigarette smoke exposure was associated with decreased risk of colorectal cancer only in NAT2 strong acetylators (OR, 2.6; 95 per cent CI, 1.1-5.9 for childhood and adult use). Frequent intake of red meat dramatically raised the risk of colorectal cancer in the community containing of NAT2 fast acetylators or NAT1*10 allele carriers (OR, 2.6; 95 per cent CI, 1.1-6.1), but not for those with NAT1 and NAT2 genotypes "late'.' Our results suggest that genotypes NAT1 and NAT2 may lead to individual susceptibility together, and that heterocyclic aromatic amines may play an significant role in colorectal cancer associated with red meat and probably even in ambient tobacco smoke exposures.

Anna L et al., 2006 [14], examined the level of alcohol and tobacco use at appearance and place of CRC. The IMPAC Health Registry Services Cancer Data Reference Report for CRCs, diagnosed between June 1, 1993 and December 31, 2003, was challenged. Such topics have been identified as present, former, or never drug and tobacco users. Use these explanatory variables along with class , ethnicity, and insurance coverage, a logistic regression model for the position of CRC and a linear regression model for age at diagnosis were built. We also researched with CRC on 161 172 cases. During the onset of the CRC, current drinking, smoking, and smoking plus alcohol is correlated with younger ages (adjusted age gap, respectively 5.2, 5.2, and 7.8 years; P<.001 for all). Current drinkers (odds ratio, 1.192; confidence interval of 95 per cent, 1.15-1.23) and smokers (odds ratio, 1.164; confidence interval of 95 percent, 1.12-1.21) were more likely to have a distal CRC position. Among men, colorectal cancer appeared to develop early (adjusted age gap, 1.9 years; P<.001) and had distal predominance (odds ratio, 1.42; P<.001) relative to women. For women the smoking but not the magnitude of the alcohol impact was higher than in men (adjusted age gap, 2.6 years; P<.001). We conclude that use of alcohol, tobacco and male gender was correlated with earlier onset and a distal CRC position.

On the basis of a longitudinal observational sample of germline mutation carriers (hMLH1 or hMSH2) from the Hereditary Cancer Institute at Creighton University, one of the oldest and highest registries of HNPCC patients, Patrice Watson et al., 2004 [15] also determined whether tobacco use would change CRC incidence in carriers of HNPCC-associated mutations. Tobacco use, hMLH1 mutation transport (as compared to hMSH2), and male sex were shown to be substantially correlated with increased CRC risk (hazard ratios, respectively 1.43, 2.07, and 1.58). Use of alcohol has not altered risk of CRC. Bu-Tian Ji, et al.,2006 [16] Studies have been performed to classify the role of tobacco in early colorectal carcinogenesis, comparing tobacco usage among 4,383 subjects with histologically confirmed benign (hyperplastic or adenomatous) distal colon polyps (descending colon, sigmoid and rectum) tobacco use among 33,667 subjects who were endoscopically negative for distal colon tumors, in the Prostate, Lung screening section, Risks estimated by the odds ratio (OR) associated with current cigarette use were OR = 4.4 [95 percent confidence interval (95 percent CI), 3.7-5.2] for hyper plastic polyps only, OR = 1.8 (95 percent CI, 1.5-2.1) for adenomas only, and OR = 6.2 (95 percent CI, 4.7-8.3) for subjects with both hyper plastic and adenomatous polyps simultaneously. Results in ex smokers were weaker; the smoking related ORs for hyper plastic polyps remained significantly higher. This trend was also seen in regards to smoked cigarettes a day, length of the smoking, and years of packaging. Additionally, when considering hyper plastic disorder, tobacco-associated chances for multiple polyps were greater. In conclusion, tobacco use, particularly recent use, increases the risk for both adenomatous and hyper plastic polyps, but the risks to hyperplastic lesions are significantly higher.

Mette Sørensen et al., 2008 [17] 379 cases of colorectal cancer (CRC) and 769 members of the sub-cohort were found in a cohort of 57,000. The associations between tobacco use, meat intake (red, processed and fried) and CRC risk were not statistically relevant. Preference for pan-fried brown-dark meat increased the risk of CRC. NAT1 fast acetylators posed a significantly higher risk of CRC than slow NAT1 acetylators, while NAT2 acetylator status did not affect the risk of CRC. In relation to the CRC risk, there were no statistically significant associations between tobacco smoking and either NAT1 or NAT2 acetylator status. Smoking intensity, however, quickly increased CRC risk among both NAT1 and NAT2 carriers. It suggests that the N-acetylator status affects the smoking / CRC-risk relationship.

Ruizhi Hou et al., 2014 [18] the association of polymorphisms in excision repair group 1 (ERCC1) (rs3212986, rs229881 and rs11615) and xeroderma pigmentosum-complementation group F (XPF) (rs2276466 and rs6498486) with risk of colorectal cancer was examined. A case – control analysis matched to 1:1 was performed. Conditional regression analysis showed that individuals carrying the genotype ERCC1 rs3212986 TT and T allele had a marginally increased risk of colorectal cancer compared with subjects carrying the genotype GG. Similarly, subjects bearing the genotype rs11615 TT and T allele had a slightly increased risk of colorectal cancer compared with those bearing the genotype CC. Stratified research showed that individuals with current or former smokers with rs3212986 TT had a substantially increased risk of colorectal cancer, and a substantial association between this SNP and cigarette smoking was found. In conclusion, our study suggests that in a Chinese population especially in smokers, rs3212986 and rs11615 polymorphisms are associated with the risk of colorectal cancer. This result could be useful in identifying the genetic features of colorectal cancer, and suggests more successful prevention and treatment approaches.

3. RISK FACTORWS OF COLORECTAL CANCER

Several factors related to diet have been linked with colorectal cancer. In addition, the associations between diet, weight and exercise and risk of colorectal cancer are among the strongest for any form of cancer.

Being overweight or obese

People are overweight or obese (severely overweight), are at greater risk of developing and dying from colorectal cancer. Getting overweight increases both men and women's risk of colon and rectal cancer, although the correlation appears to be greater in men. Keeping to a healthier weight and keeping at it will help to reduce the risk.

Not being physically active

People are not physically fit, so they are more likely to develop colon cancer. Periodic moderate to intense physical activity can help reduce your risk.

Certain types of diets

A diet rich in red meats (such as beef, pork, lamb, or liver) and fried meats (such as hot dogs and other luncheon meats) raises the chances of contracting colorectal cancer. Cooking meats at extremely high temperatures (frying, broiling, or grilling) will produce toxins that may raise the risk of cancer. Too far that may raise the risk of colorectal cancer isn't obvious. Low vitamin D levels in the blood can also increase the risk. Following a healthier lifestyle of eating with lots of fruits, vegetables and whole grains, and reducing or eliminating red and fried meats and sugar beverages, the risk is likely to be minimized.

Smoking

People who have smoked tobacco long are more likely to develop and die from colorectal cancer than non-smokers. Smoking is a well-known cause of cancer of the lung but it is linked to many other cancers.

Alcohol use

Colorectal cancer has been linked with mild to high consumption of alcohol. Only the mild to moderate consumption of alcohol has been associated with a certain harm. Doesn't drink alcohol anyway. If people do drink alcohol, men should have no more than 2 drinks a day and women should have 1 drink a day. It may have a lot of health effects like a reduced risk of cancer of various types.

Being older

The risk of colorectal cancer decreases with your age. Younger adults can get it but after age 50, it's far more likely. There is an uptick in colorectal cancer in people younger than age 50 and the cause for this is uncertain.

History of colorectal polyps or colorectal cancer

Whether the individuals have history of adenomatous polyps (adenomas), the risk of contracting colorectal cancer is increased. It is particularly true if the polyps are large, if all of them are present, or if some of them display dysplasia.

Personal history of inflammatory bowel disease

People have inflammatory bowel disease (IBD), like either ulcerative colitis or Crohn's disease, and there is an elevated chance of colorectal cancer. IBD is a long-term disease in which the bowel is inflamed. People who have had IBD for several years frequently experience dysplasia, particularly if untreated. Dysplasia is a term used to classify cells which appear irregular in the colon or rectum lining but are not cancer cells. Over time, they can transition to cancer. Inflammatory intestinal disorder differs from irritable bowel syndrome (IBS), which does not appear to raise the chance of colorectal cancer.

Family history of colorectal cancer or adenomatous polyps

Many colorectal cancers occur in people with no colorectal cancer family history. Nevertheless, as many as 1 in 3 people who experience colorectal cancer have other family members who have undergone it. Persons with a history of first-degree relative colorectal cancer (parent, child, or infant) are at elevated risk. The probability is much higher if the relative was diagnosed with cancer when they were younger than 50, or if it affects more than one relative in the first degree. For these cases the reasons for the heightened risk aren't clear. Regardless of inherited DNA, common

environmental factors or a combination of these, cancers will "run in the family." Finding family members who have adenomatous polyps is often associated with an elevated risk of colon cancer. (Adenomatous polyps are the polyps which may grow into cancer.)

Inherited syndrome

Approximately 5 percent of individuals who experience colorectal cancer have hereditary gene variations (mutations) that cause syndromes of family cancer, which may lead to illness. Lynch syndrome (hereditary non-polyposis colorectal cancer, or HNPCC) and family adenomatous polyposis (FAP) are the most prevalent inherited syndromes associated with colorectal cancer, although other, more unusual syndromes may also raise the risk of colorectal cancer.

4. TYPES OF COLORECTAL CANCER

Lynch syndrome (hereditary non-polyposis colon cancer or HNPCC)

The most severe genetic colorectal condition is the lynch condition. It makes up about 2 to 4 percent of all colorectal cancers. The condition is, in most cases, caused by an hereditary mutation in either the gene MLH1, MSH2 or MSH6, although variations in other genes may also cause Lynch syndrome. Normally these genes tend to repair damaged DNA. The cancers associated with this condition appear to arise when people are relatively young. Those with Lynch syndrome may have polyps, but they appear to have just a few. In people with this condition, the lifetime risk of colorectal cancer may be as high as 50%, but that depends on which gene is affected. People with this disorder often have a very high chance of contracting endometrial cancer (the uterine lining). Other diseases associated with Lynch syndrome include liver cancer, abdominal cancer, small intestine, pancreas, lung, thyroid, breast cancer, ureters (tubes bringing urine from the kidneys to the bladder), and bile duct. Individuals with Turcot syndrome (a unusual genetic condition) who have a mutation in one of the genes of the Lynch syndrome are at a greater risk of colorectal cancer and a particular form of brain cancer called glioblastoma.

Familial adenomatous polyposis (FAP)

FAP is caused by modifications (mutations) in the APC gene inherited by one's ancestors. FAP is responsible for around 1 per cent of all colorectal cancers. Hundreds or thousands of polyps form in a person's colon and rectum in the most severe forms of FAP, typically starting at age 10 to 12 years. Cancer typically occurs as early as age 20 in 1 or more of such polyps. At age 40 almost all patients with FAP may have colon cancer if they have not removed their colon to prevent it. Individuals with FAP are also at higher risk for stomach tumors, small intestines, pancreas, kidneys, and certain other tissues.

There are 3 sub-types of FAP:

- In **attenuated FAP** or **AFAP**, patients have fewer polyps (less than 100), and colorectal cancer tends to occur at a later age (40s and 50s).
- **Gardner syndrome** is a type of FAP that also causes non-cancer tumors of the skin, soft tissue, and bones.
- **Turcot syndrome** is a rare inherited condition in which people have a higher risk of many adenomatous polyps and colorectal cancer. People with Turcot syndrome who have the APC gene are also at risk of a specific type of brain cancer called medulloblastoma.

Rare inherited syndromes linked to colorectal cancer

- **Peutz-Jeghers syndrome (PJS):** People with this genetic disorder appear to have freckles around their mouth (and often on their hands and feet) and a special form of polyp in their digestive tract called hamartomas. These men, including many cancers such as breast, ovary, and pancreas, are at a significantly greater risk for colorectal cancer. Usually diagnosed at a younger age than usual. The cause of this disease is mutations in the gene STK11 (LKB1).
- **MUTYH-associated polyposis (MAP):** Persons with this condition develop multiple polyps of the colon. It will nearly certainly turn into cancer when carefully monitored with daily colonoscopies. These individuals are also at higher risk for many GI (gastrointestinal) tract and thyroid cancers. This condition is caused by mutations in the MUTYH gene (which includes "proofreading" the DNA and correcting errors), which sometimes leads to cancer at a younger age.

Since all of these syndromes are associated with colorectal cancer at a young age, and are often associated with other forms of cancer, it is important to classify families with these inherited syndromes. If the person is younger, it helps

doctors prescribe different actions such as tests and other prevention measures. Data on risk assessment and genetic therapy and treatment for these syndromes can be found in Colorectal Cancer genetic diagnosis, screening, and avoidance for people with a good family background.

CONCLUSION

The smoking epidemic among women over the past four decades may account for some of the pronounced increase in CRC incidence. To sum up, this supports the theory that cigarette smoking among women is a preventable cause of CRC. Smoking is related to increased mortality from CRC in both males and females. The risk of mortality from rectal and proximal colon cancer was the most pronounced among male and female smokers, respectively. Female smokers can be more susceptible to colon cancer than male smokers, and particularly to proximal colon cancer. So women may need to look beyond PA to lower their CRC risk.

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