Post-colonoscopy colorectal cancer rates in the Swedish IBD and non-IBD population: Something missed or something faster?

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Cite this article as: *Yılmaz Ürün Y, Üstündağ Y. Post-colonoscopy colorectal cancer rates in the Swedish IBD and non-IBD population: Something missed or something faster? Turk J Gastroenterol 2019; 30(9): 860-2.*

Stjärngrim J, Ekbom A, Hammar U, et al. Rates and characteristics of post-colonoscopy colorectal cancer in the Swedish IBD population: What are the differences from a non-IBD population? Gut 2019; 68(9): 1588-96.

Colorectal cancer (CRC) is the fourth most common cancer in the United States (1,2). Colonoscopic surveillance for CRC has decreased the CRC incidence and mortality in recent years, but CRC is still the second most common cause of cancer-related deaths worldwide (3,4). Colonoscopy is the recommended method for screening CRC, and it is performed every 10 years in average risk population after age 50 years. Cancerous and precancerous lesions could be detected via direct visualization by colonoscopy with >95% sensitivity for CRC and 88%-98% sensitivity for advanced adenomas (>10 mm in diameter) (5,6). The risk for CRC is higher in patients with inflammatory bowel disease (IBD), and CRC accounts for 10%-15% of all IBD deaths (7). Therefore, regular screening for CRC in patients with IBD plays a special role and needs utmost attention. Surveillance colonoscopies are recommended to start 8-10 years after the disease onset to detect premalignant lesions at an early stage (8).

A recently published article in Gut entitled "Rates and characteristics of post-colonoscopy colorectal cancer in the Swedish IBD population: what are the differences from a non-IBD population?" evaluated the rates of post-colonoscopy colorectal cancer (PCCRC) in the adult Swedish IBD population and investigated whether there is a higher rate of PCCRC in an IBD population than of PCCRC in a non-IBD population. The aim of the present study was to evaluate the pattern of associated risk factors, such as age, sex, CRC localization, CRC detection time, and comorbidities, for PCCRC and to compare the pattern in the IBD population with that of the population without IBD. For this purpose, they scanned all colonoscopies between 2001 and 2010 in Sweden on individuals 18 years or older by using the operation codes for colonoscopy and colonoscopy with biopsy from the National Hospital Discharge Register and the National Outpatient Register. Individuals who had undergone colonoscopies were linked to the Swedish Cancer Register. All individuals without a previous CRC but with a CRC within 0-36 months after a colonoscopy were selected for the study (2001-2013), regardless of whether the CRC was subsequently detected by a colonoscopy. All colonoscopies were followed up at least 36 months. PCCRC was defined as a CRC that was detected within 6-36 months after a negative index colonoscopy with regard to CRC. Thus, the colonoscopy was reported as a false-negative examination. Detected CRC (dCRC) was defined as a CRC that was detected within 6 months after a colonoscopy, and this was reported as a true-positive examination. The PCCRC rate was expressed as the number of false-negative divided by the number of true-positive and the number of false-negative colonoscopies. Overall, 348,232 colonoscopies in 270,918 patients were enrolled in the study. There were 27,123 (8%) colonoscopies that were performed on 14,597 (5%) individuals with Crohn's disease (CD), and 51,572 (15%) colonoscopies were performed on 26,513 (8%) individuals with ulcerative colitis (UC). Out of these, 269,545 colonoscopies were performed on 229,808 individuals without IBD. Of the colonoscopies during this period, 23% were performed on individuals with IBD, and 77% were performed on the non-IBD population. Overall, 13,731 cases of CRC in an interval of 0-36 months were identified during 2001-2013, out of which 133 were among individuals with CD, 281 were among individuals with UC, and 13,317 were in the non-IBD group. Additionally, age, sex, location of the cancer, stage of the cancer, and if the colonoscopy was performed in a university hospital with comorbidities, such as diabetes mellitus, ischemic heart disease (IHD), diverticulosis, primary sclerosing cholangitis (PSC), and former colorectal polyp, in an earlier colonoscopy were evaluated in the study.

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DOI: 10.5152/tjg.2019.030919

Nearly all CRCs were a PCCRC among individuals with PSC in the IBD group. Therefore, the PCCRC rates were also calculated by excluding this group, which did not influence the results substantially.

In multivariate analysis, the RR for a CRC in the IBD group to be a PCCRC compared with a CRC in the non-IBD group was 3.82 in the CD group and 5.89 in the UC group ($p<0.001$).

Additionally, the highest risk for the PCCRC was defined as younger age (especially between 30 and 40 years) in the UC group and having CRC in the rectum in the CD group.

IBD groups (especially men) were younger than the non-IBD group. Among men in the IBD group, those with PCCRCs were significantly younger than those with dCRC, but this significance could not be reached in the non-IBD group. The significant increased risk of PCCRC was detected in individuals with diverticular disease, history of a previous benign colorectal polyp, and female gender in the non-IBD group, but these risk factors were not found to be significant among the IBD groups. The presence of a polyp at a previous colonoscopy in the UC group was not found to be a risk factor for future PCCRC, whereas three times increased risk factor was observed in the non-IBD group. An explanation of this result could be that CRC in UC does not follow the classical CRC pathway as in patients with non-IBD (9).

PCCRC rates were 28.3% in the CD group, 41% in the UC group, and 6.3% in the non-IBD group. In the present study, these high PCCRC rates could be explained by some slow handling cases that are noted >6 months after the index colonoscopy although they had CRC within 6 months of the examination.

At the time of diagnosis, nearly half of the PCCRCs were diagnosed at T3 and T4 stages (CD group T3/T4:19/42, 45.2%; UC group T3/T4:71/141, 50.3%; and non-IBD group T3/T4:435/858, 50.7%). The PCCRC rates in the IBD groups are five and seven times higher than those in the non-IBD group. The high rates with more advanced stages could demonstrate that these PCCRCs actually indicate missed lesions at the index or surveillance colonoscopy, emphasizing the need for finding better surveillance strategies. Moreover, it is clear that recommendations on IBD surveillance shift from white light endoscopy with random biopsies to high definition chromoendoscopy with directed biopsies to improve the dysplasia detection rate (10,11). However, another explanation of the high rates could be that CRCs in patients with IBD grow faster than CRCs in patients with non-IBD, and contrary to international recommendations about surveillance colonoscopies in IBD, colonoscopic surveillance is not performed in endoscopic remission that causes to miss some important lesions (8,12). Additionally, the significant increased risk of PCCRC in the right-sided location of the tumor, among women and in individuals with diverticulosis and IHD, was observed in the non-IBD group, though it was not observed among those with IBD.

The PCCRC rates have been found to be 15% lower in an American study that includes elderly patients with IBD than in the present study (13). The low rates could be attributed to the calculation of the formula of the PCCRC rates because CRC was used as the dominator.

In an English study by Morris et al., the PCCRC rates have been found to be 32% for CD and 36% for UC, but the present study includes patients with IBD who had previously been hospitalized for IBD, so the high rates could be explained by the severeness of the disease because the severe disease had a higher risk of PCCRC than the mild disease (14). A recently published Dutch study by Wintjens et al. reported a PCCRC rate of 45% that is higher than other studies, but this high rate may be due to longer follow-up time (15).

Although the present study has some limitations, such as insufficient information on the extent of colitis, disease duration, previous findings of dysplasia without polyps, completeness of the index procedure, quality of bowel preparation of index colonoscopy, and characteristics of the mucosal lesions, it is a large study encompassing almost 350,000 colonoscopies.

In conclusion, different rates of PCCRC were reported by different countries, but PCCRC rates appear to be high and it is still an important issue for patients with IBD. These results showed that surveillance strategies of CRC in patients with IBD play an important role in mortality and morbidity and need high attention.

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