

Survival from Colorectal Cancer in Relation to Inflammatory Bowel Disease

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Inflammatory bowel disease (IBD), which includes ulcerative colitis and Crohn's disease, is associated with an increased risk of colorectal cancer (CRC), possibly due to increased oxidative stress and other effects of chronic inflammation. CRC cases arising in association with IBD tend to be younger than non-IBD cases, and have other clinical and molecular differences. It has also been shown that use of non-steroidal anti-inflammatory medications improves survival after diagnosis with CRC, suggesting that inflammation may affect disease progression.

This led Dr. Scott Adams and colleagues in Public Health Sciences to hypothesize that IBD-associated CRC cases have worse survival compared to non-IBD-associated CRC cases. Previous studies addressing this potential link have mostly been small and hospital-based, and have had inconsistent findings. Dr. Adams and colleagues undertook a study using the Colon Cancer Family Registry (CCFR) to compare survival and IBD-associated and non-associated CRCs.

Data on CRC diagnosis, survival, clinical data, and patient characteristics were obtained using the CCFR. Investigators identified IBD-associated cases as those CRC patients who had previously been diagnosed with either ulcerative colitis or Crohn's disease, according to their initial interview at CCFR enrollment. The investigators checked the accuracy of these data by reviewing medical records for IBD diagnosis in a subset of participants.

7,202 CRC cases were included in the study, of which 250 were IBD-associated cases. 2,013 deaths occurred in non-IBD-associated cases (29%), and 74 in IBD-associated cases (30%), 12 years after diagnosis with CRC. After accounting for differences in age at CRC diagnosis, sex, number of prior endoscopies, and CCFR phase, there was evidence of poorer 5-year survival for IBD-associated CRC compared to non-IBD-associated CRC. Specifically, IBD-associated cases were 36% more likely to die within 5 years of diagnosis than non-IBD-associated cases (hazard ratio (HR) 1.36, 95% confidence interval (CI) 1.05-1.76). Even after accounting for differences in CRC stage at diagnosis, survival was still worse in IBD-associated cases, suggesting that IBD-associated CRC progresses more quickly than non-IBD-associated CRC.

The investigators conducted additional analyses restricted to IBD diagnoses confirmed by medical record review, and stratified by duration of IBD before CRC diagnosis. Results were similar in these analyses. When looking separately at ulcerative colitis versus Crohn's disease, there was some evidence that patients with only Crohn's disease were less likely to survive to 5 years (HR: 1.74, 95% CI 1.09-2.79) than patients with only ulcerative colitis (HR 1.18, 95% CI 0.85-1.63).

Based on this study, IBD-associated CRC appears to have poorer 5-year survival than non-IBD-associated CRC. Because of limitations in the data, the investigators were unable to assess the effects of differences in treatment of CRC or IBD, or identify which IBD patients had received surveillance for CRC. They also were unable to reliably compare longer-term survival.

"I think the question [this study] raises is *why* there is a difference in survival between CRC patients where cancer develops within IBD, and "sporadic" CRC," Dr. Adams noted. He points out that perhaps IBD patients just have poorer health in general due to the seriousness of IBD, or alternatively, "Do these comorbidities [of IBD] make it difficult to complete cancer treatment? Or is there something different biologically about the tumors?"

This research group plans to follow up on this work by looking at genetic differences in the IBD-associated and non-IBD associated cancers. "We are planning to go back to the Colon CFR tumor archives and see how the mutation spectrum differs between these two types of tumors..., for important gene mutations associated with CRC." Dr. Adams notes that most previous studies of this question have been based on much smaller studies, and that the relatively large size of the CCFR will be useful.

[Adams SV, Ahnen DJ, Baron JA, Campbell PT, Gallinger S, Grady WM, Lemarchand L, Lindor NM, Potter JD, Newcomb PA.](#) 2013. Survival after inflammatory bowel disease-associated colorectal cancer in the Colon Cancer Family Registry. *World Journal of Gastroenterology* 19(21):3241-3248. doi: 10.3748/wjg.v19.i21.3241.

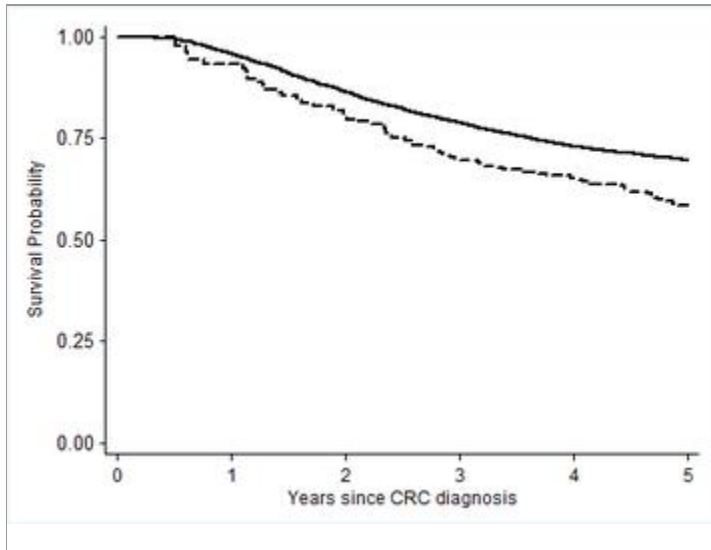


Image provided by the author

Survival probability for non-IBD-associated (solid line) and IBD-associated colorectal cancer (dashed line), after adjusting for confounders.