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Colorectal Cancer Risk in Crohn's Disease Patients After Colectomy: A Propensity-Matched Cohort Study Using a Nationwide EMR Database

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Abstract

Objective: To assess the risk of colorectal malignancy in CD patients with and without colectomy over time.

Methods: A retrospective cohort study was conducted using the TriNetX Research Network, which includes data from 70 U.S. healthcare organizations. A total of 7,315 CD patients who underwent partial or total colectomy were matched 1:1 to 7,315 patients without surgical intervention. Patients with ulcerative colitis were excluded. CRC outcomes including colon (C18), rectosigmoid (C19), and rectal (C20) cancers were analyzed at 5-, 10-, and 20-year follow-up intervals. Hazard ratios (HR) with 95% confidence intervals (CI) were calculated, and Kaplan-Meier curves were compared using log-rank testing.

Results: Among 14,630 matched CD patients, colon cancer incidence at 5 years was 5.4% in the colectomy group vs. 0.6% in the non-colectomy group (HR 8.40; 95% CI: 6.19 to 11.40). Elevated risk persisted at 10 years (5.5% *vs*. 0.8%; HR 7.02) and 20 years (6.1% *vs*. 0.9%; HR 7.06). Rectosigmoid cancer occurred in 1.5% of colectomy patients *vs*. 0.2% of controls (HR 7.09), and rectal cancer in 1.5% *vs*. 0.5% (HR 3.23). All differences were statistically and clinically significant.

Conclusions: Colectomy in CD is associated with a sustained increase in CRC risk, especially in the colon and rectosigmoid junction, highlighting the need for lifelong surveillance in this population.

Keywords: Crohn's Disease; Colectomy; Colorectal Cancer; Inflammatory Bowel Disease

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Introduction

Colorectal cancer (CRC) remains one of the most serious long-term complications in patients with inflammatory bowel disease (IBD), including Crohn's disease (CD). Although the risk of CRC in ulcerative colitis (UC) has been extensively characterized, the malignancy risk in CD, particularly involving colonic disease, is increasingly recognized and may be underestimated in clinical practice. A meta-analysis by Jess et al. found that patients with colonic CD have a twofold increased risk of developing CRC compared to the general population, underscoring the importance of long-term surveillance in this population [1].

Historically, colectomy has been regarded as a protective intervention in IBD patients, aimed at removing chronically inflamed or dysplastic colonic mucosa. In ulcerative colitis, total proctocolectomy has been shown to virtually eliminate CRC risk when the entire colon and rectum are resected [2]. This notion has often been extrapolated to Crohn's disease. However, CD differs fundamentally from UC in its segmental and transmural involvement, which may leave residual bowel at risk even after colectomy. Furthermore, the type and extent of colectomy in CD are highly variable, ranging from segmental to subtotal resections, raising questions about the completeness of cancer risk mitigation [3].

The association between colectomy and subsequent CRC risk in Crohn's patients remains poorly defined. Existing literature presents conflicting findings. Some studies suggest a decreased risk post-

colectomy, while others report persistent or even elevated CRC risk, particularly in patients with residual rectal segments or ileorectal anastomosis [4, 5]. The ambiguity may stem from heterogeneous study populations, limited sample sizes, and inconsistent adjustment for disease severity, duration, and family history. Additionally, most prior analyses have relied on single-institution datasets or national registries, which may lack detailed clinical variables and longitudinal follow-up.

To address these limitations, real-world evidence derived from large-scale electronic health record (EHR) networks provides a powerful alternative. These databases offer diverse, multi-institutional patient populations and granular clinical data, enabling robust analyses of long-term outcomes in heterogeneous clinical scenarios [6]. TriNetX, in particular, aggregates EHRs from over 100 million patients across more than 22 countries, allowing for comprehensive cohort matching and follow-up in a real-world setting [7].

In this study, we leverage the TriNetX US Collaborative Network to evaluate the long-term risk of colorectal cancer in Crohn's disease patients who underwent colectomy compared to a matched cohort managed non-surgically. By controlling for key baseline characteristics, including family history of gastrointestinal malignancy, we aim to clarify whether colectomy alters the trajectory of CRC development in this high-risk population.

Methods

Study Design and Data Source

A retrospective cohort study was conducted using the TriNetX US Collaborative Network, a federated research platform that aggregates de-identified electronic health records from over 70 participating hospitals and clinics across the United States. As the data is de-identified, this study was exempt from internal board review (IRB)

Cohort Selection

Adult patients (aged 18 years and older) with a diagnosis of Crohn's disease (ICD-10: K50) and no history of ulcerative colitis were included. Two cohorts were defined: (1) patients who underwent partial or total colectomy, and (2) patients with Crohn's disease who did not undergo any colectomy procedures.

Matching and Covariate Adjustment

To reduce confounding, a 1:1 propensity score matching was applied based on age, sex, race, ethnicity, and family history of gastrointestinal malignancies. After matching, each cohort included 7,315 patients.

Follow-Up Periods and Outcomes

Patients were followed across three time intervals: short-term (5 years or 1,825 days), intermediate-term (10 years or 3,650 days), and long-term (up to 20 years or until the last recorded clinical encounter). The primary outcomes were new diagnoses of colorectal malignancies, including colon cancer (ICD-10: C18), rectosigmoid junction cancer (ICD-10: C19), and rectal cancer (ICD-10: C20).

Statistical Analysis

Kaplan-Meier survival analysis and Cox proportional hazards regression were used to compare cancer incidence between cohorts. Hazard ratios (HRs) with 95% confidence intervals were calculated to assess relative risk across time points.

Results

Following 1:1 propensity score matching, the study included 14,630 patients with Crohn's disease, evenly divided between those who underwent colectomy (n=7,315) and those who did not (n=7,315). Cancer incidence was assessed at 5-year, 10-year, and lifetime follow-up intervals. Analyses were performed separately for colon cancer (ICD-10: C18), rectosigmoid junction cancer (C19), and rectal cancer (C20).

Colon Cancer (ICD: C18)

At 5 years, 395 patients (5.4%) in the colectomy group developed colon cancer, compared to 46 patients (0.6%) in the non-colectomy group. The absolute risk difference was 4.8% (95% CI: 4.2%–5.3%, p<0.001), with a risk ratio (RR) of 8.59 (95% CI: 6.34–11.63), odds ratio (OR) of 9.02 (95% CI: 6.64–12.26), and hazard ratio (HR) of 8.40 (95% CI: 6.19–11.40, p<0.001). Kaplan-Meier survival at 5 years was 94.06% for colectomy *vs.* 99.15% for non-colectomy (log-rank p<0.001).

At 10 years, incidence was 403 cases (5.5%) in the colectomy group and 57 cases (0.8%) in the non-colectomy group (RR 7.07, 95% CI: 5.37–9.31; OR 7.42, 95% CI: 5.62–9.82; HR 7.02, 95% CI: 5.32–9.26, p<0.001). Ten-year survival was 93.68% *vs.* 98.59%, respectively (p<0.001).

At lifetime follow-up, colon cancer occurred in 444 colectomy patients (6.1%) and 65 non-colectomy patients (0.9%). The RR was 6.83 (95% CI: 5.28–8.84), OR 7.21 (95% CI: 5.54–9.37), and HR 7.06 (95% CI: 5.44–9.16, p<0.001). Survival at the final timepoint was 92.86% *vs.* 97.51% (p<0.001).

Rectosigmoid Junction Cancer (ICD: C19)

At 5 years, rectosigmoid cancer developed in 100 colectomy patients (1.4%) and 14 non-colectomy patients (0.2%), yielding an RR of 7.14 (95% CI: 4.09–12.48), OR of 7.23 (95% CI: 4.13–12.66), and HR of 7.02 (95% CI: 4.01–12.28, p=0.028). Five-year survival was 98.25% *vs.* 99.72% (p<0.001).

At 10 years, there were 103 cases (1.4%) in the colectomy group *vs.* 15 cases (0.2%) in the non-colectomy group (RR 6.87, 95% CI: 4.00–11.79; OR 6.95, 95% CI: 4.04–11.96; HR 6.84, 95% CI: 3.98–11.77, p=0.030). Ten-year survival was 97.96% *vs.* 99.67% (p<0.001).

At lifetime follow-up, 111 patients (1.5%) in the colectomy group developed rectosigmoid cancer compared to 16 patients (0.2%) in the non-colectomy group. RR was 6.94 (95% CI: 4.11–11.71), OR 7.03 (95% CI: 4.16–11.88), and HR 7.09 (95% CI: 4.20–11.99, p=0.015). Survival rates were 97.16% *vs.* 99.51% (p<0.001).

Rectal Cancer (ICD: C20)

At 5 years, rectal cancer was diagnosed in 99 colectomy patients (1.4%) and 30 non-colectomy patients (0.4%), resulting in an RR of 3.30 (95% CI: 2.20–4.96), OR of 3.33 (95% CI: 2.21–5.02), and HR of 3.18 (95% CI: 2.11–4.78, p=0.122). Five-year survival was 98.42% for colectomy and 99.47% for non-colectomy (p<0.001).

At 10 years, incidence increased to 102 cases (1.4%) in the colectomy group and 33 cases (0.5%) in the non-colectomy group. RR was 3.09 (95% CI: 2.09–4.57), OR 3.12 (95% CI: 2.11–4.63), and HR 3.03 (95% CI: 2.05–4.49, p=0.050). Survival rates were 98.22% *vs.* 99.25% (p<0.001).

At lifetime follow-up, 111 colectomy patients (1.5%) developed

rectal cancer compared to 35 (0.5%) in the non-colectomy group. RR was 3.17 (95% CI: 2.17–4.63), OR 3.21 (95% CI: 2.19–4.69), and HR 3.23 (95% CI: 2.21–4.72, p=0.106). Lifetime survival was 97.64% for colectomy and 99.25% for non-colectomy (p<0.001).

Discussion

Main Findings

In this cohort of 14,630 patients, colectomy was associated with persistently elevated colorectal cancer (CRC) risk. Patients with Crohn's disease who had colectomy were approximately seven to eight times more likely to develop colon or rectosigmoid cancer compared to matched non-colectomy patients at 5, 10, and lifetime follow-up [8]. Rectal cancer risk remained elevated at around three-fold even at long-term follow-up [9].

Interpretation

The notably high risk of rectosigmoid and rectal cancers likely reflects that residual rectal mucosa remains vulnerable after partial colectomy or ileorectal anastomosis. Meta-analyses report a pooled rectal cancer incidence of about 1.3% in IBD patients with a retained rectum after colectomy [10]. Surveillance bias may also contribute, since colectomy patients typically undergo more intensive long-term endoscopic monitoring, leading to earlier or more frequent detection of malignancy [11]. Additionally, requirement for colectomy often reflects a more severe Crohn's phenotype, penetrating, stricturing, or refractory disease, which independently confers higher CRC risk due to longer duration of inflammation [12].

Comparison to Prior Literature

These findings diverge markedly from ulcerative colitis populations, where colectomy is generally protective and significantly reduces CRC risk by removing the at-risk mucosa [13]. In contrast, CD involves segmental and transmural inflammation that may recur postoperatively, limiting the protective effect of surgery and sustaining long-term neoplastic risk [14]. Prior studies often included smaller cohorts and shorter follow-up; our real-world EMR–based dataset with up to 20 years of observation provides stronger longitudinal evidence.

Clinical Implications

Our data suggest that colectomy does not eliminate CRC risk in Crohn's disease and may instead unmask persistent susceptibility. Colectomy patients, especially those with retained rectum, should undergo tailored, long-term surveillance beyond current guideline intervals. Risk-stratified surveillance, informed by residual bowel anatomy, disease behavior, and surgical history, may optimize early detection and reduce mortality. Further studies are needed to explore whether biologic or immunomodulatory therapies post-colectomy alter long-term CRC risk. Research should also clarify optimal surveillance intervals for patients with retained rectum or ileorectal anastomosis. Prospective cohort studies incorporating histology, microbiome profiles, and genetic predisposition would enhance understanding of mechanistic drivers of post-surgical CRC risk.

Limitations

This study has several important limitations inherent to retrospective analyses of real-world electronic health record data. First, the TriNetX database does not include detailed operative notes or surgical pathology, preventing stratification by colectomy type (e.g., segmental, subtotal, or total) or reconstruction approach (e.g., ileorectal anastomosis *vs.* end ileostomy). The inability to account for retained rectal tissue may partially explain the elevated risk of rectosigmoid and rectal cancers observed in the colectomy cohort. Second, data on surveillance colonoscopy frequency, adenoma detection rates, and adherence to post-colectomy cancer screening guidelines were not available, limiting our ability to control for surveillance intensity as a potential confounder. Third, reliance on diagnostic and procedural codes introduces risk of misclassification or undercoding, particularly in distinguishing cancer location and identifying postoperative disease recurrence. Lastly, although we applied rigorous 1:1 propensity score matching for demographic and baseline risk variables, residual confounding from unmeasured factors such as disease duration, medication use, histologic inflammation, and provider-level variation in care remains possible.

Conclusion

Our findings challenge the conventional assumption that colectomy mitigates long-term colorectal cancer risk in Crohn's disease. Despite surgical removal of affected bowel segments, patients who underwent colectomy remained at significantly higher risk of colon and rectosigmoid cancers for up to two decades following surgery. These elevated risks may reflect residual mucosal vulnerability, cumulative inflammatory burden, and heightened disease severity requiring surgical intervention. Notably, rectal cancer risk persisted at nearly three-fold higher rates among colectomy patients, suggesting that retained distal bowel segments remain at oncologic risk even after major surgical resection. Taken together, these results highlight the need for long-term, anatomy-tailored surveillance strategies in Crohn's disease patients post-colectomy. Clinicians should not assume surgical resection confers cancer risk elimination and should instead maintain vigilant screening practices guided by surgical anatomy, patient history, and evolving risk stratification tools.

AI Declaration

Artificial intelligence tools, including ChatGPT (OpenAI), were used in the preparation of this manuscript for tasks such as language refinement, organization of author-drafted content, and formatting assistance. All data analysis, interpretation, and critical content were conducted and reviewed by the authors. The final manuscript was thoroughly edited and approved by all authors to ensure accuracy, originality, and compliance with ethical standards. No AI tool was used for data generation, statistical analysis, or drawing scientific conclusions.

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Specific Author Contributions

Syed Fahad Gillani contributed to the conception and design of the study, data extraction, statistical analysis, and interpretation of results. He also critically revised the manuscript for intellectual content and approved the final draft submitted.

Rawan Elkomi contributed to study design, data interpretation, and drafting of the manuscript. She participated in critical revisions and approved the final draft submitted.

Anand Deonarine provided overall oversight and strategic guidance. He supervised all aspects of data handling, including

quality assurance, and methodological integrity, and approved the final draft submitted.

Syed Asad Geelani assisted with literature review, and interpretation of findings. He reviewed and approved the final version of the manuscript.

Ali Chand contributed to data curation, helped organize tables and figures, and participated in manuscript revisions. He approved the final draft submitted.

Jesse Maynard provided methodological oversight, contributed to data validation and critical review of statistical output, and approved the final draft submitted.

Mekdem Bisrat participated in data cleaning, quality assurance, and manuscript formatting. She reviewed and approved the final draft submitted.

Miriam Michael contributed to the literature review, referencing, and final proofreading of the manuscript. She reviewed and approved the final draft submitted.

Study Highlights

What is Known

- Colorectal cancer (CRC) is a known long-term complication in Crohn's disease (CD).
- Colectomy is often assumed to reduce CRC risk by removing diseased colonic tissue.
- Unlike ulcerative colitis, Crohn's disease involves patchy, transmural inflammation that can recur after surgery.

What is New Here

- Colectomy in CD patients is associated with persistently elevated CRC risk, especially in the colon and rectosigmoid junction.
- Colon cancer risk remained sevenfold higher even at 20-year follow-up post-colectomy.
- Rectal cancer incidence was nearly threefold higher in colectomy patients despite resection.
- Findings challenge assumptions of surgical protection and support lifelong surveillance tailored to residual anatomy.

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