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Colorectal Cancer Risk in Ulcerative Colitis Patients With and Without Colectomy: A Propensity-Matched Cohort Study

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Abstract

Background & Aims: The long-term risk of colorectal neoplasia in ulcerative colitis (UC) patients undergoing colectomy remains poorly quantified. This study compared the incidence of colorectal malignancies in UC patients with versus without colectomy across 5-year, 10-year, and 20-year follow-up.

Methods: Using the TriNetX US Collaborative Network, we conducted a propensity score-matched cohort study of 3,767 UC patients with colectomy (partial/total) and 3,767 non-colectomy UC controls, matched for age, sex, race, and family cancer history. Outcomes included incident colon (C18), rectosigmoid (C19), and rectal (C20) cancers analyzed at 5-year, 10-year, and 20-year intervals. Risk ratios (RR), hazard ratios (HR), and survival probabilities were calculated.

Results: Colectomy patients had significantly higher risks of colorectal cancers. Colon cancer incidence was 20.0% at 5 years (*vs*. 1.6%, HR 13.2), persisting through 10 and 20 years. Rectosigmoid cancer risk peaked at 5 years (HR 20.4), remaining elevated at 20 years (HR 14.4). Rectal cancer risk was consistently increased (HR range 7.4–8.3). 20-year survival was significantly lower in colectomy patients.

Conclusions: Colectomy for UC is associated with a markedly increased risk of colorectal malignancy, particularly in the first 5 years for colon cancer and persistently for rectosigmoid and rectal cancers. Lifelong surveillance is warranted post-colectomy.

Keywords: Ulcerative Colitis; Colectomy: Colorectal Cancer; Inflammatory Bowel Disease; Cancer Surveillance

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Introduction

Ulcerative colitis (UC) is a chronic, idiopathic inflammatory condition of the colonic mucosa that typically begins in the rectum and extends proximally in a continuous fashion [1]. It is characterized by periods of relapse and remission and affects approximately 1 million people in the United States [2]. UC is strongly associated with an increased risk of colorectal cancer (CRC), primarily due to chronic mucosal inflammation leading to dysplasia and neoplastic transformation [3].

Multiple epidemiologic studies have documented this elevated cancer risk. The risk of CRC in UC patients increases with longer disease duration, greater extent of colonic involvement, and higher inflammatory burden [4]. In a meta-analysis of 116 studies, Eaden et al. found that the cumulative risk of CRC reached 18% after 30 years of UC duration [5].

Historically, colectomy has been regarded as a definitive intervention to mitigate CRC risk in UC patients [6]. Total proctocolectomy with ileal pouch-anal anastomosis (IPAA) is often performed in patients with high-grade dysplasia or medically refractory disease [7]. The rationale for this surgical approach is to eliminate dysplasia-prone colonic mucosa, thereby removing the primary site of carcinogenesis.

However, recent data challenge the assumption that colectomy eliminates CRC risk. Retained

rectal or rectosigmoid segments, often preserved in subtotal colectomy or incomplete proctectomy, may continue to harbor inflammation, dysplasia, or carcinoma [8]. Furthermore, chronic inflammation of the ileal pouch or retained rectal stump has been associated with neoplastic changes [9].

Several studies have reported carcinoma arising in the pouch or residual rectal segments years after colectomy, indicating that malignancy risk may persist long after surgical resection [10]. Despite this, existing literature has been limited by small cohort sizes, variable surgical definitions, and short follow-up intervals [11].

There remains a critical need for large-scale, real-world data to clarify long-term CRC risk following colectomy in UC. To address this gap, we conducted a retrospective cohort study using the TriNetX research network to evaluate the incidence of colon, rectosigmoid, and rectal cancers among UC patients treated with and without colectomy. Outcomes were assessed at 5-year, 10-year, and 20-year follow-up intervals to provide a comprehensive view of long-term malignancy risk.

Methods

Study Design and Data Source

This was a retrospective cohort study conducted using the TriNetX U.S. Collaborative Network, a federated health research platform aggregating de-identified electronic medical record (EMR) data from over 70 U.S. healthcare organizations [12]. TriNetX enables large-scale observational research by allowing for real-time analyses across a diverse patient population. All data were HIPAA-compliant and de-identified before researcher access.

Cohort Selection

Eligible participants were adult patients aged 18 years or older with a confirmed diagnosis of ulcerative colitis (UC), identified using ICD-10 code K51. The study period spanned from January 1, 2000, to January 1, 2024. Patients with a diagnosis of Crohn's disease (ICD-10: K50) were excluded.

Two study cohorts were created: a colectomy group and a non-colectomy group. Colectomy patients were identified using CPT codes 44140 through 44208, encompassing both partial and total colectomy procedures. For the colectomy cohort, the index event was the first recorded colectomy. For the non-colectomy group, the index event was the date of UC diagnosis.

Matching and Covariate Adjustment

Propensity score matching was performed using a 1:1 nearest-neighbor algorithm without replacement. Covariates included in the matching model were age at index, sex, race, ethnicity, and family history of digestive malignancies. This approach aimed to minimize confounding and simulate a randomized comparative framework. After matching, both cohorts comprised 3,767 patients each, yielding a total analytic sample of 7,534 individuals.

Follow-Up Periods and Outcomes

The study assessed the incidence of colorectal cancer at three prespecified follow-up intervals: 5 years, 10 years, and 20 years from the index event. Outcomes of interest included new diagnoses of:

- Colon cancer (ICD-10: C18)
- Rectosigmoid junction cancer (ICD-10: C19)
- Rectal cancer (ICD-10: C20)

Each malignancy was recorded based on the first instance of diagnostic coding following the index event. Patients were censored at death or loss to follow-up.

Statistical Analysis

Survival analyses were performed using Kaplan-Meier methods to estimate time-to-event for each cancer outcome. Cox proportional hazards models were used to calculate hazard ratios (HRs) with 95% confidence intervals (CIs). Risk ratios (RRs), odds ratios (ORs), and absolute risk differences were computed for incidence comparisons at each time point. The log-rank test was employed to compare survival distributions between cohorts, with statistical significance set at $\alpha = 0.05$.

Results

Following propensity score matching, a total of 7,534 patients with ulcerative colitis were included in the analysis, comprising 3,767 patients who underwent colectomy and 3,767 matched controls who did not receive surgical intervention. Cancer incidence and survival outcomes were evaluated at three time points: 5-year, 10-year, and 20-year follow-up intervals.

Colon Cancer (ICD-10 C18)

At the 5-year follow-up, colon cancer was diagnosed in 752 out of 3,767 patients (19.9%) in the colectomy group compared to 62 out of 3,767 (1.6%) in the non-colectomy group. This yielded a risk difference of 18.3% (95% CI: 17.0%–19.7%, $p < 0.001$), a risk ratio (RR) of 12.13 (95% CI: 9.40–15.65), and an odds ratio (OR) of 14.91 (95% CI: 11.45–19.40). The survival probability was lower in the colectomy group at 78.98%, compared to 97.81% in the non-colectomy group. The hazard ratio (HR) was 13.20 (95% CI: 10.19–17.11, $p < 0.001$).

At the 10-year interval, 755 colectomy patients (20.0%) developed colon cancer compared to 68 (1.8%) in the control group. The risk difference was 18.2% (95% CI: 16.9%–19.6%, $p < 0.001$), RR was 11.10 (95% CI: 8.70–14.17), and OR was 13.64 (95% CI: 10.59–17.56). The survival probabilities were 78.53% for colectomy and 97.03% for controls, with an HR of 12.14 (95% CI: 9.47–15.56, $p < 0.001$).

Over the 20-year follow-up, 756 colectomy patients (20.1%) were diagnosed with colon cancer versus 68 (1.8%) in the non-colectomy cohort. The absolute risk difference remained at 18.3% (95% CI: 16.9%–19.6%, $p < 0.001$), RR was 11.12 (95% CI: 8.71–14.19), and OR was 13.66 (95% CI: 10.61–17.59). The survival probability dropped further to 77.89% in the colectomy group versus 97.03% in controls, with a corresponding HR of 12.17 (95% CI: 9.50–15.60, $p < 0.001$).

Rectosigmoid Junction Cancer (ICD-10 C19)

At 5 years, 216 of the colectomy patients (5.7%) were diagnosed with rectosigmoid cancer, compared to 11 (0.3%) in the control group. This represented a risk difference of 5.4% (95% CI: 4.7%–6.2%, $p < 0.001$), an RR of 19.64 (95% CI: 10.73–35.93), and an OR of 20.77 (95% CI: 11.31–38.13). Survival was 93.04% for colectomy patients versus 99.66% for non-colectomy patients, with an HR of 20.36 (95% CI: 11.11–37.32, proportionality $p = 0.895$).

By 10 years, 217 colectomy patients (5.8%) developed rectosigmoid cancer versus 15 (0.4%) of controls. The risk difference remained 5.4% (95% CI: 4.6%–6.1%, $p < 0.001$), RR was 14.47 (95% CI: 8.59–24.37), and OR was 15.29 (95% CI: 9.04–25.85). Survival probabilities were 92.88% versus 99.07%, and HR was 15.12 (95% CI: 8.96–25.52, $p = 0.015$).

At 20 years, 218 colectomy patients (5.8%) and 16 non-colectomy patients (0.4%) were diagnosed with rectosigmoid cancer, corresponding to a risk difference of 5.4% (95% CI: 4.6%–6.1%, $p < 0.001$), RR of 13.63 (95% CI: 8.22–22.59), and OR of 14.40 (95% CI: 8.65–23.98). Survival was markedly reduced in the colectomy group (61.92%) compared to 98.54% in the control group. The HR was 14.40 (95% CI: 8.66–23.93, $p = 0.009$).

Rectal Cancer (ICD-10 C20)

For rectal cancer, 248 colectomy patients (6.6%) developed malignancy at 5 years compared to 30 (0.8%) in the non-colectomy group. The absolute risk difference was 5.8% (95% CI: 4.9%–6.6%, $p < 0.001$), RR was 8.27 (95% CI: 5.68–12.04), and OR was 8.78 (95% CI: 5.99–12.86). The survival probability was 92.76% in the colectomy cohort versus 99.09% in the control cohort, with an HR of 8.49 (95% CI: 5.81–12.40, proportionality $p = 0.192$).

At the 10-year mark, 250 colectomy patients (6.6%) developed rectal cancer versus 33 controls (0.9%). The risk difference remained at 5.8% (95% CI: 4.9%–6.6%, $p < 0.001$), RR was 7.58 (95% CI: 5.28–10.86), and OR was 8.04 (95% CI: 5.58–11.60). Survival was 92.49% in the colectomy group and 98.62% in the non-colectomy group. The HR was 7.84 (95% CI: 5.45–11.26, $p = 0.013$).

Over 20 years, 250 colectomy patients (6.6%) and 34 non-colectomy patients (0.9%) were diagnosed with rectal cancer. The absolute risk difference was 5.7% (95% CI: 4.9%–6.6%, $p < 0.001$), RR was 7.35 (95% CI: 5.15–10.49), and OR was 7.81 (95% CI: 5.44–11.20). Survival probability in the colectomy group was 92.49%, compared to 98.15% in the non-colectomy group, and the HR was 7.62 (95% CI: 5.33–10.91, $p = 0.005$).

Discussion

This large-scale, real-world analysis of over 7,500 patients provides compelling evidence that colectomy in ulcerative colitis (UC) does not eliminate the risk of colorectal cancer (CRC), and may in fact be associated with persistently elevated malignancy risk across all assessed anatomic sites and time intervals. Most notably, colon cancer incidence in the colectomy cohort remained significantly higher than in non-colectomy controls at 5 years (752/3,767 *vs.* 62/3,767), 10 years (755/3,767 *vs.* 68/3,767), and 20 years (756/3,767 *vs.* 68/3,767). These findings challenge the conventional assumption that colectomy is a protective intervention against future CRC.

One possible explanation for the increased risk is the presence of residual at-risk tissue following partial or subtotal colectomy. Studies have shown that retained rectal or rectosigmoid segments can remain susceptible to chronic inflammation, dysplasia, and malignant transformation even after surgical intervention [13]. Moreover, inflammation in ileal pouch-anal anastomoses or the presence of pouchitis has also been implicated in long-term neoplasia risk, although such risks have historically been considered lower than in native colon [14].

Our data further revealed that rectosigmoid and rectal cancers occurred at significantly higher rates in the colectomy cohort. At 20-year follow-up, the incidence of rectosigmoid cancer was 218/3,767 compared to only 16/3,767 in non-colectomy patients, and for rectal cancer, the figures were 250/3,767 versus 34/3,767. These findings emphasize that even distal colonic resection does not fully mitigate the risk, and suggest the need for ongoing endoscopic surveillance even in the absence of a native colon.

These results are consistent with prior reports demonstrating increased risk of neoplasia following restorative procedures such as ileorectal anastomosis or IPAA [15, 16]. Although colectomy reduces the bulk of colonic mucosa, it does not eliminate all carcinogenic risk, particularly in cases where rectal or distal colon segments are retained.

The implications of these findings are clinically significant. Physicians may need to reconsider the long-held belief that surgical resection renders patients free from future cancer risk. Instead, patients who undergo colectomy, especially those with retained segments or incomplete resections, should be enrolled in lifelong surveillance protocols. These might include regular endoscopic evaluations and careful monitoring for signs of inflammation or dysplasia.

Finally, while this study provides strong evidence for elevated CRC risk post-colectomy, it does not address the biological mechanisms driving these outcomes. Future studies investigating mucosal biomarkers, genetic predispositions, and postoperative inflammatory states may help explain why colectomy fails to provide the expected oncologic protection in UC patients.

Clinical Implications

The findings of this study have substantial clinical implications for the management of ulcerative colitis (UC). Historically, colectomy has been considered a curative or prophylactic intervention for patients at high risk of colorectal cancer (CRC), particularly those with dysplasia or refractory disease. However, the persistent and elevated CRC risk identified in this study challenges that paradigm. These results suggest that colectomy does not offer complete oncologic protection and that malignant transformation may continue in residual mucosa, especially in patients undergoing subtotal colectomy or restorative procedures like ileorectal anastomosis or ileal pouch-anal anastomosis (IPAA). Clinicians should exercise caution when counseling patients about the long-term cancer risks following surgery. Postoperative surveillance strategies must be maintained indefinitely, particularly for patients with retained rectal or rectosigmoid segments. Risk stratification, shared decision-making, and close endoscopic monitoring should remain central components of post-colectomy care.

Limitations

This study should be interpreted in the context of its limitations. First, its retrospective design using electronic medical record (EMR) data is susceptible to documentation and coding inaccuracies, which may affect diagnostic validity. Second, key clinical variables such as disease extent, medication history (e.g., use of biologics or immunomodulators), histologic inflammation, and dysplasia status were not available, limiting the ability to adjust for potential confounding factors. Third, there may be an element of selection or indication bias, wherein patients undergoing colectomy may have had more severe disease or a higher pre-existing malignancy risk. Although propensity score matching accounted for demographic and familial risk factors, unmeasured confounding may still influence the observed associations. Finally, this study did not assess cancer staging, treatment outcomes, or cause-specific mortality, which could provide more granular insight into post-colectomy cancer prognosis.

Conclusion

In this large, real-world matched cohort study of UC patients, colectomy was associated with a significantly elevated and persistent

risk of colorectal cancer, particularly in the colon, rectosigmoid junction, and rectum, over a 20-year follow-up period. These findings call into question the traditional assumption that colectomy is protective against CRC and highlight the need for continued vigilance and surveillance in post-surgical patients. Surgical decisions should be individualized, and clinicians must recognize that cancer risk endures long after colectomy, especially in those with retained distal bowel segments. Future research is warranted to elucidate the biological mechanisms driving post-colectomy neoplasia and to refine risk-based surveillance strategies in this population.

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.

Specific Author Contributions

Rawan Elkomi: Conceptualization, study design, data acquisition, drafting of manuscript, critical revision for important intellectual content. She has read and approved the final manuscript.

Syed Fahad Gillani: Data curation, statistical analysis, interpretation of data, manuscript writing, and editing. He has read and approved the final manuscript.

Daniel Larbi: Literature review, drafting of the introduction and discussion, figure and table preparation. He has read and approved the final manuscript.

Jesse Maynard: Senior oversight, guidance on study design, and critical review of the final manuscript. He has read and approved the final manuscript.

Rana Elkomi: Quality control of data and methodology, interpretation of results, and manuscript revision. She has read and approved the final manuscript.

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

Elizabeth Beyene: Verification of data integrity, statistical methods validation, and proofreading. She has read and approved the final manuscript.

Miriam Michael: Supervision, methodology review, and final approval of the version to be published. She has read and approved the final manuscript.

Study Highlights

What Is Known

- Ulcerative colitis increases long-term colorectal cancer risk, especially with prolonged inflammation and disease duration.
- Colectomy is traditionally believed to lower colorectal cancer risk in ulcerative colitis patients.
- Long-term cancer risk after colectomy is poorly studied in large, real-world UC populations.

What Is New

- Colectomy was linked to increased cancer incidence at 5-, 10-, and 20-year follow-up.
- Risk remained highest for colon and rectosigmoid junction cancers after surgery.
- Colectomy does not eliminate cancer risk in ulcerative colitis patients.
- Lifelong colorectal cancer surveillance is necessary after colectomy, especially with retained rectal segments.

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