

Crohn's versus Cancer: Comparison of Functional and Surgical Outcomes after Right-Sided Resections

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Keywords

Crohn's disease · Right colectomy · Outcome

Abstract

Background: The objective of this study was to compare functional and surgical outcomes of patients undergoing ileocecal resection for Crohn's disease (CD) to patients undergoing oncological right colectomy. **Methods:** Retrospective single-center cohort study including consecutive patients undergoing right colectomy for adenocarcinoma (oncological resection) or CD (mesentery-sparing resection) between July 2011 and November 2017. Outcome measures were pathological details (lymph node yield), postoperative recovery (pain levels, return to flatus and stool, intake of fluids, weight change, and mobilization), and early (30-day) outcomes (surgical/medical complications, hospital stay, readmissions). **Results:** A total of 195 patients (153 [78%] with cancer and 42 [22%] with CD) were included. Overall compliance with the institutional enhanced recovery protocol was comparable between the 2 groups (compliance $\geq 70\%$: 60% in CD patients vs. 62% in cancer, $p = 0.458$). The adenocarci-

noma group had a larger lymph node yield than the CD group (26 ± 13 vs. 2.4 ± 5 , respectively, $p < 0.001$). While the CD group experienced significantly more pain ($3.7 \pm 1.9/10$ vs. $2.8 \pm 2.5/10$, $p = 0.007$, patients requiring opioids: 65 vs. 28%, $p = 0.001$), return of flatus (2.3 ± 1.2 days vs. 2.4 ± 2.8 days, $p = 0.642$) and stool (4.1 ± 6.0 vs. 3.0 ± 1.8 days, $p = 0.292$) was no different in both groups. No difference was observed regarding postoperative complications, length of stay, and readmission rate. **Conclusion:** This study revealed no differences in both functional and surgical outcomes in CD and cancer patients undergoing mesentery-sparing or formal oncological right colectomy, respectively.

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Introduction

Crohn's disease (CD) is an immune-mediated chronic disease that can affect any segment of the digestive tract and features transmural invasion and fistula formation [1]. Despite being a non-curative disease, more than half of patients need surgical treatment for medi-

cally refractory inflammation leading to acute (i.e., perforation) or chronic (i.e., stricture) complications [2]. With 58%, the ileocecal segment is the most prevalent primary location of the disease and may require ileocecal resection for disease control [3, 4]. Formal right colectomy is the standard approach to right-sided colon cancer, in which a central resection with high ligation of the ileocolic axis is mandatory for complete removal of tumor-draining lymphovascular tissue. Conversely, CD typically needs less radical resection of lymphovascular structures and is mainly guided by the extent of the inflammatory process.

Because the Abbreviated Injury Scale for mesenteric injury in traumatology reflect a supposed increased risk of small bowel obstruction, central resection of the ileocolic pedicle and its neurovascular structures may have a negative impact on recovery of bowel function [5, 6]. On the other hand, wide mesentery-including resections have been suggested in patients with CD for better control of disease recurrence [7–9]. The objective of this study was to compare functional recovery and surgical outcomes in patients undergoing mesentery-sparing ileocecal resection for CD to patients undergoing oncological right colectomy to explore whether wider mesenteric resections in CD may harm patient outcome.

Methods

This is a retrospective cohort study with data deriving from the enhanced recovery after surgery (ERAS) database of the Department of Visceral Surgery at Lausanne University Hospital (CHUV). Consecutive patients undergoing right colectomy or ileocecal resection for either primary, histology-proven stage I–III adenocarcinoma, or CD with an established preoperative diagnosis between July 2011 and November 2017 were included.

Demographic information included age, gender, American Society of Anesthesiologists (ASA) and World Health Organization (WHO) mobility performance scores (WHO 0: fully active, able to carry on all pre-disease performance without restriction–WHO 5: dead), BMI, social habits including active smoking and alcohol abuse (as defined by Diagnostic and Statistical Manual of Mental Disorders [DSM-5] coding) at the time of surgery, immunosuppressive medications (i.e., chemotherapy or steroids within 12 weeks of surgery), previous history of abdominal surgery, and postoperative nausea or vomiting. Surgical information included surgical approach (either open or minimally invasive, including preemptive or reactive conversion to laparotomy), elective or emergency (within 72 h of unplanned admission) indication, length of the operation (from anesthesia induction until skin closure), and length of the incision (<10 vs. >10 cm).

For CD patients, a bowel-close resection was performed. All cancer patients underwent a radical D2-lymphadenectomy yielding proximal and distal resection margins of at least 5 cm. Com-

plete mesocolic excision preserving the mesocolic plane and central ligation of the ileocolic vessels at their origin were performed routinely [10]. Anastomoses in both groups were performed in a standardized side-to-side anisoperistaltic stapling technique or an isoperistaltic side-to-side hand-sewn technique.

The institutional ERAS protocol has been previously described [11]. Compliance to individual ERAS items was calculated using the previously described critical cutoff of 70% (overall compliance) for comparative purposes [12].

Outcomes

Functional outcomes included postoperative pain levels, assessed by visual analog scales (VAS 0: no pain 10: highest pain intensity) and opioid use at postoperative day (POD) 0–3 for adequate pain control, time from surgery to return to flatus and stool, postoperative oral intake of fluids (L/24 h), postoperative weight change (POD 1–3 compared to preoperative weight), and postoperative mobilization (hours/day, POD 1–3). Postoperative complications were assessed according to the Clavien classification [13] (with major complications defined as \geq grade III) and included infectious (surgical site infection and medical infectious including urinary tract infection and pneumonia), respiratory (atelectasis) and cardiovascular complications (arrhythmias, deep venous thrombosis, pulmonary embolism), urinary retention (need for in/out catheterization), anastomotic leakage (clinically or radiologically confirmed), postoperative length of stay (surgery to discharge), readmission (to either index or independent facility), and postoperative ileus (POI) or small bowel obstruction. POI was defined as postoperative reinsertion of a nasogastric tube after removal at the end of anesthesia. Small bowel obstruction was defined as the need of reoperation. For the purpose of this study, both entities were combined.

Specific Assessments for Oncological and Crohn's Patients

For oncological patients, distal, proximal, and vascular pedicle tumor resection margins and total, peritumoral, and central lymph nodes were reviewed by specialized institutional pathologists [14]. For CD patients, preoperative medical therapy including corticosteroids, immunomodulators (azathioprine and methotrexate), and biologic molecules (adalimumab, certolizumab, infliximab, vedolizumab, and ustekinumab), which were stopped at minimal drug half-life time (at least 10–25 days), except for emergency surgical indications, were analyzed. Surgical indication (medically refractory or complicated disease: stenosis, fistula, and perforation), need of oncological resection (high-tie of the ileocolic axis), and total number of resected lymph nodes were also assessed.

Statistical Analysis

Descriptive statistics were reported as frequency and percentages and continuous variables were reported as mean (SD) or median (interquartile range–IQR). χ^2 test was used for categorical variables and Student's *t* test for continuous variables. Variables with a *p* value <0.05 indicate statistical significance. Statistical analyses were performed with the Statistical Software for the Social Sciences SPSS Advanced Statistics 22 (IBM Software Group, 200 W. Madison St., Chicago, IL 60606, USA) and GraphPad Prism Software 8 (2365 Northside Dr., Suite 560, San Diego, CA 92108, USA).

Table 1. Demographics and surgical details

Item	All patients (n = 195)	Crohn's (n = 42)	Cancer (n = 153)	p value
Age (mean ± SD), years	64±20	37±15	71±14	<0.001
>70 years, n (%)	97 (50)	1 (2)	96 (63)	<0.001
Gender (male), n (%)	100 (51)	24 (57)	76 (50)	0.486
ASA group (III–IV), n (%)	65 (33)	3 (7)	62 (41)	<0.001
WHO performance score (≥2), n (%)	45 (23)	7 (17)	38 (25)	0.306
BMI (mean±SD), kg/m ²	25±6	23±5	26±6	0.001
>25 kg/m ² , n (%)	85 (44)	12 (29)	73 (48)	0.035
Smoker, n (%)	40 (21)	13 (31)	27 (18)	0.083
Alcohol, n (%)	15/155 (10)	14/120 (12)	1/35 (3)	0.193
Immunosuppression, n (%)	41 (21)	33 (79)	8 (5)	<0.001
Previous abdominal surgery, n (%)	54 (28)	8 (19)	46 (30)	0.177
Previous PONV, n (%)	14/189 (7)	4 (10)	10/147 (7)	0.517
Minimally invasive approach, n (%)	155 (79)	38 (90)	117 (76)	0.053
Conversion, n (%)	7/155 (5)	2/38 (5)	5/117 (5)	0.683
Emergency indication, n (%)	49 (25)	7 (17)	42 (27)	0.167
Duration of operation (mean±SD), min	150±70	140±60	150±70	0.194
>180 min, n (%)	55 (28)	10 (24)	45 (29)	0.564
Hand-sewn anastomosis, n (%)	23 (12)	4 (10)	19 (12)	0.789
Incision > 10 cm, n (%)	75/189 (40)	10/41 (24)	65 (44)	0.030

All conversions from laparoscopy to laparotomy were done preemptively. Baseline demographic parameters of patients with CD (n = 42) and patients with adenocarcinoma (n = 153) undergoing ileocecal resection or right colectomy. Bold p values indicate statistical significance (p < 0.05). CD, Crohn's disease; ASA, American Society of Anesthesiology; WHO, World Health Organization performance score; PONV, postoperative nausea and vomiting; SD, standard deviation.

Results

A total of 195 patients (153 [78%] with cancer and 42 [22%] with CD) were included. Oncological patients were older, sicker (ASA score), and had higher BMI scores, as outlined in Table 1. There were no differences in social habits, WHO performance scores, and previous surgery or postoperative nausea or vomiting history between both groups. While CD patients were more often operated by minimally invasive approach (90 vs. 76%, p = 0.053), the conversion rate (all pre-emptive) was comparable. Most anastomoses (n = 172, 88%) were configured in an anisoperistaltic stapled fashion with equal distribution between both groups.

Compliance with the Enhanced Recovery Protocol

Overall compliance with the ERAS protocol was similar between the 2 groups (≥70%: 62% in cancer vs. 60% in CD patients, p = 0.458). Significant differences were observed in intraoperative EDA use and postoperative opioid use within 48 h (see online suppl. material; see www.karger.com/doi/10.1159/000509748 for all online suppl. material). Further specifics of CD and cancer patients re-

garding preoperative immunosuppressive treatments and pathological details are summarized in Tables 2 and 3. The adenocarcinoma group had a larger lymph node yield than the CD group (26 ± 13 vs. 2.4 ± 5 respectively, p < 0.001).

Functional Outcome

Return of flatus was 2.3 ± 1.2 days in CD versus 2.4 ± 2.8 days in cancer patients, p = 0.642, while return of stool was 4.1 ± 6.0 days in CD versus 3.0 ± 1.8 days in cancer patients. The CD group experienced significantly more pain at POD 0, POD 1, POD 2, and POD 3, as shown by both increased VAS scores and increased use of opioid medication through POD 3 (Fig. 1). Oncological patients gained significantly more weight (POD 2 and 3), while no differences in postoperative mobilization and oral intake were observed.

Surgical Outcome

Infectious, cardiovascular, respiratory, abdominal, urinary, and anastomotic complication rates were similar in both groups (Table 4). No difference was observed for length of stay and readmission rate.

Table 2. Specifics Crohn's patients

Item	N (%)
Crohn's medication	
Corticosteroids	12 (29)
>20 mg	4 (10)
Immunomodulator	
AZA	7 (17)
MTX	1 (2)
Biologic therapy	
ADA	10 (24)
CTZ	2 (5)
IFX	5 (12)
VED	6 (14)
UST	1 (2)
Surgical indication	
Medically refractory	8 (19)
Stenosing disease	36 (86)
Fistulizing disease	7 (17)
Perforating disease	2 (5)
Pathologic details	
Oncologic resection	0
Total lymph nodes (mean±SD)	2.4±5

Preoperative treatments, surgical indications, and pathologic specifics of Crohn's patients ($n = 42$). AZA, azathioprine; MTX, methotrexate; ADA, adalimumab; CTZ, certolizumab; IFX, infliximab; VED, vedolizumab; UST, ustekinumab; SD, standard deviation.

Discussion

Despite more central resection and as expected increased lymph node yield in cancer patients and similar compliance to the perioperative care protocol, recovery of bowel function did not differ between both groups. While CD patients experienced more postoperative pain, no differences were observed in postoperative complications, length of stay, and readmissions. Based on these data, more extensive resection in CD patients to prevent disease recurrence may be warranted and will most likely not negatively impact functional recovery.

Surgery is obviously not a curative treatment for CD. Endoscopic recurrence occurs in 30% at 1 year and 85% at 3 years after surgery, while clinical recurrence at 1 year occurs in 8–20% [15–17]. Furthermore, surgical recurrence occurs in 30% of patients at 10 years [18, 19]. High visceral fat area and high mesenteric fat index are associated with postoperative recurrence at 6 months [20]. Coffey et al. [8] evaluated the rate of surgical recurrence between conventional, mesentery-sparing ileocolic resections for CD and those including a wide mesenteric

Table 3. Specifics adenocarcinoma patients

Item	Mean ± SD
Lymph nodes (n)	
Total	26±13
Positive total	2±4
Peritumoral	14±9
Positive peritumoral	3±4
Central	12±9
Positive central	1±2
Tumor margin, cm	
Distal (colonic)	10.2±5.6
Proximal (ileal)	9.8±6.1
Vascular pedicle	7.5±4
R0 resection, n (%)	152 (99)

Pathologic details of patients with adenocarcinoma ($n = 153$). SD, standard deviation.

resection and demonstrated that retention of the mesentery was an independent predictor of surgical recurrence. In their study, the rate of surgical recurrence was 40% after conventional ileocolic resection against 2.9% with wide excision of the mesentery. Therefore, mesenteric resection was suggested as an efficient technique to decrease postoperative recurrence since widespread resection was linked to a higher lymph node yield and thus reduction of potential immunologic reactions. The authors also explained the beneficial effect of mesenteric resection by assuming that it reduces the local recruitment of fibrocytes. The percentage of fibrocytes correlated with the mesenteric disease severity, which in turn correlated to the CD activity index and the mucosal disease activity index. Furthermore, mesenteric resection was associated with reduced intestinal resection and margin positivity rate.

However, the role of mesentery in CD is still matter of debate, as some authors suggested an immunological protection of fat wrapping [21, 22]. According to their data, radical mesenteric resection could lead to poorer clinical outcomes. Furthermore, resection of the mesentery is associated with a non-negligible risk of bleeding, which can cause major peri- and postoperative complications [9]. In the present study, mesenteric resection did not lead to increased overall or specific postoperative complications. For this reason, the results may support a more extended surgical approach in CD. However, whether the mesentery has an immunological protection or not, in ileocecal CD, needs to be determined by further studies.

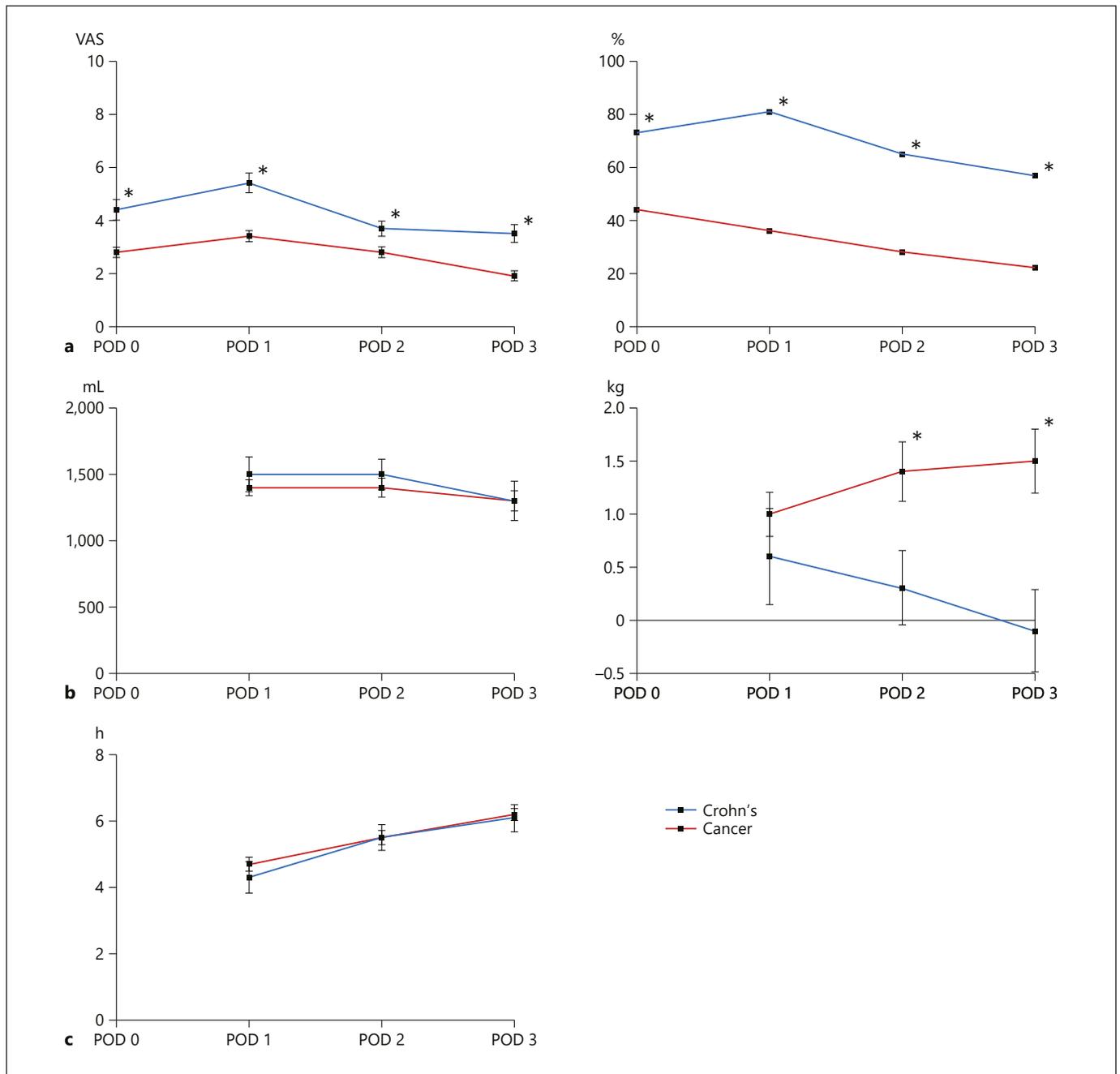


Fig. 1. Functional outcome, postoperative pain, oral intake and weight, and mobilization. Comparison of postoperative pain scores (left) and percentage of patients needing opioid medication (right) (a), oral fluid intake (left) and weight change (right) (b), and mobilization of patients with CD ($n = 42$, blue lines) (c) and

patients with adenocarcinoma ($n = 153$, red lines). CD, Crohn's disease; VAS, visual analog scale; POD, postoperative day; SEM, standard error of the mean. * Indicates statistical significance ($p < 0.05$). Displayed are means (squares) with SEM.

Mascarenhas et al. [23] analyzed short-term outcomes after ileocolic resection and right hemicolectomies for CD patients compared with non-Crohn's comparative group and showed no differences in postoperative needs

for surgical re-intervention and POI. They concluded that the underlying pathology does not influence surgical outcomes, similar as the present study, which focused in particular on functional outcomes. However, recent stud-

Table 4. Surgical outcome

Outcome	All patients (<i>n</i> = 195)	Crohn's (<i>n</i> = 42)	Cancer (<i>n</i> = 153)	<i>p</i> value
Any complication, <i>n</i> (%)	87 (45)	20 (48)	67 (44)	0.727
Major complication (Clavien ≥ III), <i>n</i> (%)	16 (8)	2 (5)	14 (9)	0.530
Infectious complication, <i>n</i> (%)	31 (16)	6 (14)	25 (16)	1.000
POI/SBO, <i>n</i> (%)	34 (17)	8 (19)	26 (17)	0.756
Respiratory complication, <i>n</i> (%)	16 (8)	1 (2)	15 (10)	0.201
Cardiovascular complication, <i>n</i> (%)	6 (3)	0	6 (4)	0.334
UTI, <i>n</i> (%)	6 (3)	0	6 (4)	0.344
Urinary retention, <i>n</i> (%)	13 (7)	4 (10)	9 (6)	0.483
Anastomotic leak, <i>n</i> (%)	4 (2)	1 (2)	3 (2)	0.512
LoS, days (median, IQR)	5 (3, 8)	5 (3, 7)	6 (3, 8)	0.087
Readmission, <i>n</i> (%)	16/190 (8)	3/40 (8)	13/150 (8)	1.000

POI, postoperative ileus; SBO, small bowel obstruction; UTI, urinary tract infection; LOS, length of stay.

ies revealed delayed GI function associated with colectomy for inflammatory bowel disease [24, 25]. Dai et al. [24] suggested preoperative conditioning (normalization of albumin levels, steroid weaning) and early management of postoperative sepsis as efficient measures to reduce POI.

In the present analysis, CD patients, who were younger than the comparative cancer group, experienced significantly more postoperative pain. Preoperative chronic pain and young age have been repeatedly identified as risk factors for increased postoperative pain [26, 27]. Arguably, chronic abdominal pain is a major concern in CD patients [3]. While preoperative pain intensity was not assessed in the present study, both subjective (VAS scores) and objective (opioid consumption) measures were used to evaluate postoperative pain. Reasons for higher postoperative pain scores are multifold and may also depend on pain assessment, according to Gagliese et al. [28] who showed that VASs were not sensitive enough to detect age differences compared to other instruments. However, our assessment also revealed significant differences in opioid requirements in the younger CD cohort.

This present study showed further increased weight gain in oncological patients, potentially due to less water retention in younger patients as a result of decreased intraoperative IV fluid administration, increased postoperative ambulation, and better general capacity to eliminate excess fluids in the younger CD cohort. Interestingly, ERAS compliance overall did not differ between both groups, further supporting feasibility of ERAS care in all age-groups [29].

This study has several limitations related to the retrospective study design. The modest sample size impeded case matching to account for the heterogeneity of the comparative cohorts and is based on a single-center experience, which, however, allowed comparison within highly standardized perioperative and surgical care. Thus, our results need independent confirmation by adequately powered prospective studies comparing extended and non-extended resection, ideally solely in CD patients in a randomized fashion. Opioid consumption was not associated with poorer functional outcome. However, the dosage was not specified. Long-term results were not yet available in this study but are needed to assess the true impact of extended resection on CD recurrence. In conclusion, this study revealed no differences in both functional and surgical outcome in CD and cancer patients undergoing mesentery sparing or formal oncological right colectomy, respectively.

Statement of Ethics

This research complies with internationally accepted standards for research practice and reporting. Written informed consent was obtained from included patients, and all data were de-identified and anonymized prior to analysis. The local institutional review board approved this study (Commission cantonale d'éthique de la recherche sur l'être humain CER-VD No. 2017-01971), which was conducted in accordance with the STROBE criteria (<https://stroke-statement.org>).

Conflict of Interest Statement

All authors have no conflicts of interest to declare.

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Author Contributions

Conception and design: D.H., E.Z., F.G., N.D., and M.H. Acquisition of data: E.Z., F.G., C.B., D.H., and A.S. Analysis and interpretation of data: F.G., E.Z., and D.H. Drafting: F.G., E.Z., D.H., M.H., and N.D. Critical revision and final approval: all authors.

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