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Retrospective Cohort Study

Short-term and long-term outcomes of laparoscopic vs open ileocolic resection in patients with Crohn's disease: Propensity-score matching analysis

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Abstract

BACKGROUND

Laparoscopic ileocolic resection (LICR) is the preferred surgical approach for primary ileocolic Crohn's disease (CD) because it has greater recovery benefits than open ICR (OICR).

AIM

To compare short- and long-term outcomes in patients who underwent LICR and OICR.

METHODS

Patients who underwent ICR for primary CD from 2006 to 2017 at a single tertiary center specializing in CD were included. Patients who underwent LICR and OICR were subjected to propensity-score matching analysis. Patients were propensity-score matched 1:1 by factors potentially associated with 30-d perioperative morbidity. These included demographic characteristics and disease- and treatment-related variables. Factors were compared using univariate and multivariate analyses. Long-term surgical recurrence-free survival (SRFS) in the two groups was determined by the Kaplan-Meier method and compared by the log-rank test.

RESULTS

During the study period, 348 patients underwent ICR, 211 by the open approach and 137 laparoscopically. Propensity-score matching yielded 102 pairs of patients. The rate of postoperative complication was significantly lower (14% versus 32%, $P = 0.003$), postoperative hospital stay significantly shorter (8 d versus 13 d, $P =$

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0.003), and postoperative pain on day 7 significantly lower (1.4 *versus* 2.3, $P < 0.001$) in propensity-score matched patients who underwent LICR than in those who underwent OICR. Multivariate analysis showed that postoperative complications were significantly associated with preoperative treatment with biologics [odds ratio (OR): 3.14, $P = 0.01$] and an open approach to surgery (OR: 2.86, $P = 0.005$). The 5- and 10-year SRFS rates in the matched pairs were 92.9% and 83.3%, respectively, with SRFS rates not differing significantly between the OICR and LICR groups. The performance of additional procedures was an independent risk factor for surgical recurrence [hazard ratio (HR): 3.28, $P = 0.02$].

CONCLUSION

LICR yielded better short-term outcomes and postoperative recovery than OICR, with no differences in long-term outcomes. LICR may provide greater benefits in selected patients with primary CD.

Key Words: Crohn's disease; Laparoscopic; Surgery; Postoperative complications; Recurrence; Propensity score; Retrospective study

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Core Tip: The laparoscopic approach to ileocolic resection can be safely performed in patients with primary Crohn's disease (CD), resulting in fewer postoperative complications, faster postoperative recovery, and non-inferior surgical recurrence rate when compared with open surgery. Postoperative complications were significantly associated with preoperative use of biologics and open ileocolic resection. Additional procedures were found to be independent risk factors for surgical recurrence in patients with CD.

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INTRODUCTION

Ileocolic resection (ICR) is the most frequently performed operation for patients with abdominal Crohn's disease (CD) with involvement of the terminal ileum. Since the introduction of laparoscopic colectomy in 1991, experience with laparoscopic ICR (LICR) for CD has increased[1,2]. LICR has become the preferred surgical approach for primary ileocolic CD because it shows greater recovery benefits than open ICR (OICR). These benefits include reduced pain, lower rates of overall morbidity, shorter hospital stay, earlier return to full activity, lower costs, and improved quality of life and cosmesis compared with OICR[1-7].

Conventionally, patients with penetrating type or complex CD have not been candidates for laparoscopic surgery, with open surgery remaining the generally accepted approach for these patients. The laparoscopic approach is regarded as more technically challenging than open surgery in CD patients with complex features, including huge phlegmons, multiple enteric fistulas, and dense adhesions, as well as those requiring repeated surgery[8]. In addition, patients with complex CD have higher rates of host related risks, such as homeostasis disturbance, infection, and severe malnutrition prior to surgery caused by external or internal fistulas[9]. Therefore, utilization of LICR in patients with complex CD remains problematic.

In South Korea, the number of laparoscopic operations in CD patients has increased dramatically, from 11.6% in 2009 to more than 31% in 2015[10]. Although our institution is the highest volume center for CD in South Korea, laparoscopic surgery for CD was conservative, with performance increasing since 2014.

The present study compared the short- and long-term outcomes of LICR and OICR in patients with primary CD over a 12-year period. To overcome possible selection bias, patients in the two groups were analyzed after propensity-score matching.

MATERIALS AND METHODS

Patients and clinical variables

Patients who underwent LICR or OICR for primary CD at Asan Medical Center in Seoul, Korea, from January 2006 to December 2017, were retrospectively identified. Ileocolic resection included patients undergoing resection of the ileum and colon with ileocolic anastomosis within the right/transverse colon. Patients who underwent previous bowel resection for CD, those without anastomosis, those with ileocolic anastomosis distal to the transverse colon, and patients with missing data or loss to follow-up were excluded (Figure 1). Patients who initially underwent laparoscopic surgery but required conversion to open surgery were included in the intention-to-treat analysis. Factors recorded from patients' electronic medical records and charts included demographic characteristics, preoperative disease characteristics, operative details, and perioperative outcomes. Demographic characteristics included patient sex, age at time of surgery, body mass index (BMI), duration of disease from the time of diagnosis, smoking history, and comorbidities. Preoperative disease characteristics included Montreal classification at the time of surgery[11], extra-intestinal manifestations of disease, family history of CD, history of perianal CD, previous history of abdominal surgery, and specific history of intestinal resection for CD. Operative details included intraoperative findings from operation reports (adhesions, strictures, intestinal fistulas, abscesses, phlegmons), indications for surgical intervention, conversion to open surgery, diverting stoma, estimated blood loss, intraoperative red blood cell (RBC) transfusion, operation time, urgent surgery, and American Society of Anesthesiologists (ASA) score. Perioperative outcomes included intraoperative and postoperative morbidity and mortality within 30 d after surgery, readmission, reoperation, length of hospital stay, pain scale, and time to recovery of bowel function [12]. Additional variables included preoperative hemoglobin and albumin levels, preoperative CD medications, anastomosis configuration (side-to-side, end-to-side, side-to-end, or end-to-end), type of anastomosis (stapled or hand-sewn), and synchronous additional surgical procedures. Postoperative morbidity was graded according to the Clavien-Dindo classification. The study protocol was approved by the Institutional Review Board of Asan Medical Center (approval number: 2019-0972).

Definitions

Comorbidities included hypertension, diabetes mellitus, and others. Major intraoperative bleeding was defined as intraoperative hemorrhage reported in operation notes and requirement for transfusion of packed RBCs. However, postoperative transfusion without a need for surgical intervention was not regarded as a postoperative complication. Anemia was defined as hemoglobin concentrations < 11.5 g/dL in women and < 13 g/dL in men, and hypoalbuminemia was defined as albumin concentrations < 3.5 g/dL according to institutional guidelines. Details of additional, concomitant procedures were limited to intra-abdominal surgery, whereas perianal procedures were excluded. Recovery of bowel movement was defined as the day of first flatus.

Laparoscopic or open surgery was selected for each patient according to surgeon preference. A history of previous abdominal surgery with or without bowel resection was an important consideration when choosing the surgical method. Because patients with previous bowel resection were excluded, multiple factors such as age, general condition, and disease extent were taken into consideration. Anastomosis configurations were classified as side-to-side, end-to-side, side-to-end, and end-to-end. Anastomosis materials were categorized as stapled and hand-sewn. ICR involves the removal of the ileocecal valve and was categorized as right colectomy or ileocecal resection depending on the involvement of the hepatic flexure of the colon.

Preoperative CD medications were divided into four categories: Systemic steroids, biologics [infliximab (Remicade®, Janssen Biotech, Inc., Horsham, PA, United States) or adalimumab (Humira®, AbbVie Inc. Chicago, IL, United States)], immunomodulators (azathioprine, 6-mercaptopurine, or methotrexate), and anti-inflammatory agents (5-aminosalicylate acid or budesonide). Preoperative treatment with steroids and anti-inflammatory agents was defined as the administration of each medication within 1 mo before surgery. Treatment with biologics was defined as the administration of at least one infusion of anti-TNF agents within 3 mo before surgery, whereas treatment with immunomodulators was defined as administration within 2 mo before surgery [5]. Immunosuppressive medications included steroids, biologics, and immunomodulators, but not anti-inflammatory agents.

Complications within the first 30 postoperative days included inadvertent intraoperative injury, anastomosis leak, fistula formation, prolonged postoperative ileus,

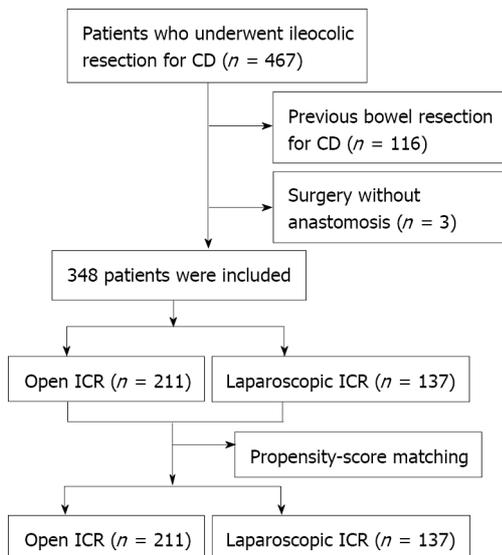


Figure 1 Flow chart of patient selection and propensity-score matching. CD: Crohn's disease; ICR: ileocolic resection.

wound or intra-abdominal infection requiring antibiotics or drainage, readmission, or return to the operating room. Septic complications included anastomosis leakage, abdominal abscess, and resulting sepsis or septic shock. Ileus was defined as the absence of bowel function by postoperative day 5 and/or the need for nasogastric tube insertion due to abdominal distension, nausea, or vomiting, without evidence of mechanical bowel obstruction.

Surgical recurrence was defined as a repeat operation on any part of the bowel for pathologically confirmed CD or for pathologically confirmed anastomotic disease, including manifestations of the small bowel at the anastomosis or stoma site. Operations not performed to treat CD exacerbations (*e.g.*, adhesiolysis or stoma closure only) were not considered reoperations for surgical recurrence.

Propensity score matching analysis

To minimize the impact of selection bias for the surgical approach and potential confounding in this observational study, patients who underwent LICR and OICR were subjected to propensity-score matching, with rigorous adjustment for significant differences in patient characteristics. Propensity scores were estimated by multiple logistic regression analysis. All pre-specified covariates were included in the full non-parsimonious models. The covariates included demographic characteristics (age, gender, BMI, smoking history, previous history of abdominal surgery, previous history of comorbidity, and ASA score), disease-related variables (Montreal classification, disease duration, perianal CD, family history of CD and extra-intestinal CD manifestations), and treatment-related variables (preoperative hemoglobin and albumin concentrations, preoperative RBC transfusions, preoperative medications, and indications for surgery). These variables were selected because they can affect the choice of surgical approach and perioperative outcomes. The operative approach was entered into the regression model as a dependent variable. A 1:1 "nearest neighbor", case-control match without replacement was used. The discrimination and calibration abilities of the propensity-score model were 0.7332 by C-statistics and $P = 0.1219$ by Hosmer-Lemeshow statistics. Following propensity-score matching, short- and long-term results were compared in the two groups.

Statistical analysis

Continuous variables were reported as mean \pm standard deviation (SD) or as median (min, max) and compared by *t*-tests or Wilcoxon rank sum tests, whereas categorical variables were reported as frequency (%) and compared by Pearson's χ^2 test or Fisher's exact test.

Univariate analyses were performed to assess the risk factors associated with postoperative complications and surgical recurrence. Multivariable models were created to identify factors independently associated with postoperative complications. Surgical recurrence-free survival (SRFS) was calculated using the Kaplan-Meier method and compared using log-rank tests. Multivariate analyses to assess the risk

Table 1 Patient demographic and clinical characteristics

	All patients			Propensity-score matched patients		
	Open (n = 211)	Laparoscopy (n = 137)	P	Open (n = 102)	Laparoscopy (n = 102)	SMD
Age (yr)	29.2 ± 9.7	29.2 ± 9.0	0.976	28.8 ± 9.0	28.6 ± 8.7	-0.026
Gender, male	153 (72.5)	95 (69.3)	0.546	78 (76.5)	72 (70.6)	-0.134
BMI (kg/m ²)	18.8 ± 3.2	18.9 ± 2.8	0.822	19.0 ± 3.3	18.9 ± 2.8	-0.041
Any smoking history	41 (19.4)	33 (24.1)	0.348	21 (20.6)	20 (19.6)	-0.025
Previous abdominal surgery	23 (10.9)	10 (7.3)	0.349	10 (9.8)	8 (7.8)	-0.069
Montreal classification						
Behavior			< 0.001			-0.044
Inflammatory (B1)	2 (0.1)	2 (1.5)		2 (2.0)	2 (2.0)	
Stricturing (B2)	38 (17.5)	52 (38.0)		30 (29.4)	26 (25.5)	
Penetrating (B3)	172 (82.0)	83 (60.6)		70 (68.6)	74 (72.5)	
Location			0.218			-0.060
Terminal ileal (L1)	68 (32.2)	50 (36.5)		36 (35.3)	37 (36.3)	
Colonic (L2)	10 (4.7)	2 (1.5)		6 (5.9)	2 (2.0)	
Ileocolic (L3)	133 (63.0)	85 (62.0)		60 (58.8)	63 (61.8)	
Disease duration (mo)	49.8 ± 50.9	68.1 ± 59.3	0.003	61.5 ± 57.4	67.0 ± 57.8	0.095
Perianal CD	103 (48.8)	57 (41.6)	0.226	45 (44.1)	45 (44.1)	0.000
Family history of CD	5 (2.4)	5 (3.6)	0.523	4 (3.9)	4 (3.9)	0.000
Extra-intestinal CD manifestation	31 (14.7)	18 (13.1)	0.754	13 (12.7)	10 (9.8)	-0.093
Comorbidity						
Hypertension	21 (10.0)	5 (3.6)	0.036	2 (2.0)	4 (3.9)	0.116
Diabetes mellitus	4 (1.9)	0 (0.0)	0.157	1 (1.0)	0 (0.0)	
Others	2 (0.9)	1 (0.7)	1.000	0 (0.0)	1 (1.0)	
ASA score, 3-4	15 (7.1)	5 (3.6)	0.239	1 (1.0)	4 (3.9)	²
Emergency	7 (3.3)	2 (1.5)	0.397	3 (2.9)	2 (2.0)	
Emergency	17 (8.1)	9 (6.6)	0.680	6 (5.9)	7 (6.9)	0.040
Preoperative data						
Hemoglobin (g/dL)	11.5 ± 1.5	11.5 ± 1.9	0.780	11.4 ± 1.4	11.4 ± 1.8	0.037
Albumin (g/dL)	3.1 ± 0.5	3.2 ± 0.5	0.140	3.1 ± 0.5	3.2 ± 0.5	0.075
Transfusion	40 (19.0)	26 (19.0)	1.000	22 (21.6)	20 (19.6)	²
Preoperative medications						
Steroids	44 (20.9)	25 (18.2)	0.584	22 (21.6)	15 (14.7)	-0.179
Immuno-modulators	96 (45.5)	67 (48.9)	0.583	48 (47.1)	50 (49.0)	0.039
Biologics	29 (13.7)	26 (19.0)	0.229	17 (16.7)	16 (15.7)	-0.027
Indication for surgery			< 0.001			
¹ Fistula <i>versus</i> others	83 (39.3)	34 (24.8)	0.022	33 (32.4)	32 (31.4)	0.021
² Obstruction <i>versus</i> others	39 (18.5)	54 (39.4)	< 0.001	31 (30.4)	26 (25.5)	-0.042

¹Fistula and obstruction were both selected in some patients.

²These variables were excluded from the propensity-score matched set because of the small numbers.

Results are reported as mean ± SD or as number (%). SMD: Standardized mean difference; BMI: Body mass index; CD: Crohn's disease; ASA: American Society of Anesthesiologists.

factors associated with SRFS were performed using Cox proportional hazards model with 95% confidence interval (CI). All statistical analyses were performed using the Statistical Package for the Social Sciences, version 24.0 for Windows (SPSS, IBM Corp., Armonk, NY, United States), with *P* values < 0.05 considered statistically significant.

RESULTS

Patient characteristics, matching, and operative details

A total of 467 patients underwent ICR for CD during the study period. Of these, 119 were excluded, including three patients without anastomosis or with ileocolic anastomosis distal to the transverse colon and 116 patients who had previously undergone bowel resection for CD. Of the 348 eligible patients, 211 underwent OICR and 137 underwent LICR. Patient characteristics before and after propensity-score matching are summarized in [Table 1](#). Compared with patients who underwent OICR for CD, those who underwent LICR had significantly lower rates of penetrating behavior ($P < 0.001$) and comorbidities ($P = 0.036$), longer disease duration ($P = 0.003$), a higher rate of surgical indication of obstruction ($P < 0.001$), and a lower rate of fistula as a surgical indication ($P = 0.022$). Crohn's Disease Activity Index (CDAI) scores were compared between the two groups. LICR and OICR groups had moderate CDAI scores (230.8 ± 9.5 and 269.1 ± 10.8 , respectively). Because the demographic data differed between the OICR and LICR groups, these patients were subjected to 1:1 propensity-score matching to reduce selection bias. A total of 102 pairs was therefore included in the propensity-score matched population.

A comparison of the propensity-score matched groups showed that the rate of intraoperative transfusion was significantly lower ($P = 0.017$), and the length of small bowel resection significantly shorter ($P < 0.001$), in the LICR than in the OICR group. Three patients (2.9%) in the OICR group, but none in the LICR group, underwent a diverting ileostomy. Although most patients in both groups underwent side-to-side anastomosis, end-to-side anastomosis was more frequently performed in the LICR than in the OICR group ($P = 0.014$). The open conversion rate in the LICR group was 4.9%. The reasons for open conversion were adhesions in two patients, huge phlegmons in two, and an abscess in one ([Table 2](#)).

Short-term outcomes

Of the 348 CD patients who underwent ICR, 75 (21.6%) experienced complications within 30 d, but none died. Of the 204 matched patients, 47 (23%) experienced postoperative complications, with 15 cases being classified as class III Clavien-Dindo complications. All six patients who required reoperation had undergone OICR, including three for anastomotic leakage and one each for an intra-abdominal abscess, luminal bleeding, and a surgical wound complication.

The overall complication rate was significantly lower in the LICR than in the OICR group (13.7% *versus* 32.4%, $P = 0.003$). The rates of septic complications, including intra-abdominal abscess ($P = 0.035$) and/or anastomosis leakage ($P = 0.014$), were also lower in the LICR group. In addition, the rates of reoperation ($P = 0.029$) and blood transfusion ($P = 0.021$) were significantly lower, hospital stay ($P = 0.003$) significantly shorter, and postoperative pain on postoperative day 7 significantly lower ($P < 0.001$) in the LICR than in the OICR group ([Table 3](#)).

Univariate analysis showed that an open approach ($P = 0.003$), previous abdominal surgery ($P = 0.037$), preoperative use of biologics ($P = 0.023$), additional procedures ($P = 0.050$), and longer operation time (> 135 min) ($P = 0.016$) were associated with postoperative complications. In multivariate analysis, an open approach [odds ratio (OR): 2.86; 95%CI: 0.17-0.73; $P = 0.005$], previous abdominal surgery (OR: 3.61; 95%CI: 1.23-10.60, $P = 0.020$), preoperative use of biologics (OR: 3.14; 95%CI: 1.33-7.40; $P = 0.009$), and longer operation time (> 135 min) (OR: 2.38; 95%CI: 1.17-4.84; $P = 0.017$) were found to be independent risk factors for postoperative complications ([Table 4](#)).

Sixteen patients experienced septic complications, 15 in the OICR and one in the LICR group. Preoperative use of steroids (OR: 4.19; 95%CI: 1.19-14.71; $P = 0.025$) and fistula as a surgical indication (OR: 4.03; 95%CI: 1.23-13.22; $P = 0.021$) were significantly associated with septic complications, whereas preoperative use of biologics was not. The laparoscopic approach was also associated with a lower risk of septic complications (OR: 0.06; 95%CI: 0.01-0.45; $P = 0.007$).

Table 2 Operative details of propensity-score matched patients

	Open (n = 102)	Laparoscopy (n = 102)	P
Operation time (min)	136.6 ± 4.5	130.4 ± 2.7	0.241
Estimated blood loss (mL)	201.8 ± 19.2	145.7 ± 22.1	0.057
Intraoperative transfusion	13 (12.7)	3 (2.9)	0.017
Diverting ileostomy	3 (2.9)	0 (0.0)	0.246
Anastomosis configuration			0.014
Side-to-side	89 (87.3)	74 (72.5)	
End-to-side	9 (8.8)	26 (25.5)	
Side-to-end	3 (2.9)	1 (1.0)	
End-to-end	1 (1.0)	1 (1.0)	
Stapled anastomosis	100 (98.0)	101 (99.0)	1.000
Operation type			0.322
Right colectomy	48 (47.1)	40 (39.2)	
Ileocecal resection	54 (52.9)	62 (60.8)	
Additional procedure	40 (39.2)	30 (29.4)	0.184
Strictureplasty	16 (15.7)	11 (10.8)	
Small bowel resection	20 (19.6)	19 (18.6)	
Colon resection	4 (3.9)	0 (0.0)	
Length of small bowel resected (cm)	60.6 ± 4.2	43.9 ± 2.8	0.001

Results are reported as mean ± SD or as number (%).

Long-term outcomes

The median follow-up duration was 74.8 mo for all patients, 88.13 mo in the OICR group, and 61.45 mo in the LICR group. By the end of the study period, 21 patients (10.3%) in the propensity-score matched cohort had experienced surgical recurrence of CD, including 14 (13.7%) who underwent OICR and seven (6.9%) who underwent LICR; these included 12 patients with fistula/abscess, four with perforation, and five with stricture. The median time to surgical recurrence was 70.3 mo for all patients, 81.7 mo in the OICR group, and 58.9 mo in the LICR group.

The overall 5- and 10-year SRFS rates were 92.9% and 83.3%, respectively, in the 204 propensity-score matched patients, 92.6% and 82.4%, respectively, in the OICR group, and 92.8% and 84.3%, respectively, in the LICR group. Kaplan-Meier analysis showed that the difference between the two groups was not statistically significant ($P = 0.407$, [Figure 2](#)). Univariate analysis showed that preoperative treatment with biologics ($P = 0.024$), side-to-side anastomosis ($P = 0.042$), and additional procedures ($P = 0.049$) were associated with surgical recurrence. Multivariate analysis revealed that the performance of simultaneous additional procedures was a risk factor for surgical recurrence [hazard ratio (HR): 3.28; 95%CI: 1.20-8.91; $P = 0.020$; [Table 5](#)].

DISCUSSION

This propensity-score matched case-control study compared short and long-term outcomes of LICR and OICR for primary CD at a single tertiary center specializing in CD. The results confirmed that LICR can be safely performed in these patients, resulting in a lower rate of postoperative complications, faster postoperative recovery, and non-inferior surgical recurrence rate compared with open surgery.

The laparoscopic approach is the preferred surgical approach for simple CD, as it is associated with a lower postoperative morbidity rate, a shorter hospital stay, earlier return to full activity, and improved quality of life[1-4]. Laparoscopic surgery is being performed more frequently in patients with complex or recurrent CD, with ran-

Table 3 Short-term outcomes of the propensity-score matched patients

	Open (n = 102)	Laparoscop (n = 102)	P	OR	95%CI	P
Total complications	33 (32.4)	14 (13.7)	0.003	0.379	0.189-0.759	0.006
Intra-abdominal abscess	8 (7.8)	1 (1.0)	0.035			
Anastomotic leakage	7 (6.9)	0 (0.0)	0.014			
Wound complication	12 (11.8)	4 (3.9)	0.065			
Ileus	2 (2.0)	7 (6.9)	0.170			
Bleeding	7 (6.9)	2 (2.0)	0.170			
Other	0 (0.0)	2 (2.0)	0.498			
Septic complications ¹	15 (14.7)	1 (1.0)	< 0.001	0.091	0.012-0.704	0.006 ^a
Reoperation	6 (5.9)	0 (0.0)	0.029	0.107	0.006-2.039	0.121 ^a
Readmission	4 (3.9)	2 (2.0)	0.689	0.250	0.053-1.177	0.109 ^a
Recovery of bowel movement (d)	2.97 ± 1.0	2.82 ± 1.0	0.295	0.971	0.694-1.359	0.864
Duration of NPO (d)	4.2 ± 1.9	3.5 ± 2.2	0.026	0.573	0.400-0.820	0.002
Total hospital stay (d)	20.7 ± 17.3	16.1 ± 8.3	0.016	0.594	0.404-0.875	0.008
Postoperative hospital stay (d)	13.1 ± 16.3	8.2 ± 3.3	0.003	0.443	0.298-0.660	< 0.001
Pain scale (NRS)						
POD#1	5.1 ± 2.0	4.9 ± 1.9	0.458	0.386	-0.183-0.956	0.181
POD#2	3.9 ± 1.8	3.9 ± 2.1	0.756	0.159	-0.392-0.710	0.567
POD#3	3.8 ± 2.1	3.3 ± 1.8	0.057	0.602	0.00-1.198	0.048
POD#7	2.3 ± 1.9	1.4 ± 1.4	< 0.001	0.628	0.156-1.100	0.010
Postoperative transfusion	23 (22.5)	10 (9.8)	0.021	0.278	0.103-0.748	0.011

¹Septic complications, including intra-abdominal abscess and anastomosis leakage.

^aExact test. Results are reported as mean ± SD or as number (%).

NRS: Numeric Pain Rating Scale; NPO: Nothing Per Oral; POD: Postoperative day; OR: Odds ratio; CI: Confidence interval.

domized-controlled studies and meta-analyses providing evidence that LICR is safe and effective, even in patients with severe CD[5-7]. The present study showed that LICR was associated with a lower rate of postoperative complications, a shorter postoperative hospital stay, and reduced postoperative pain, with no difference in the behavior or severity of CD. These results support recent trends showing that LICR may be feasible in selected patients with CD.

Operation time was comparable in the LICR and OICR groups. Although several studies have reported that operation time is longer for laparoscopic than for open surgery[1,13,14], other studies have found that operation time is shorter for LICR than for OICR[15,16]. Our finding, of no difference in operation time between laparoscopic and open surgery, may have been due to lack of calibration of selection, even after propensity-score matching. For example, the resected length of the small bowel differed between the LICR and OICR groups, and additional procedures were more frequent in patients who underwent open surgery.

The present study found that preoperative use of corticosteroids was associated with higher rates of intra-abdominal abscess and anastomosis leakage. Moreover, preoperative treatment with biologics was associated with a higher risk of short-term complications. These results are similar to those of the large observational TREAT registry ($n = 6273$), in which use of infliximab and corticosteroid increased the risks of serious infection[17-19]. In addition, our study found that a history of previous abdominal surgery was associated with postoperative complications. The specific impact of previous intestinal resection on postoperative complications in patients with CD has not been determined. One study reported that 47.6% of postoperative complications occurred in patients with a history of previous abdominal surgery ($n = 10$, $P = 0.310$), although the difference was not statistically significant[20]. Other studies have found that previous abdominal surgery is a significant risk factor for postoperative

Table 4 Univariate and multivariate regression analyses of risk factors associated with postoperative complications in propensity-score matched patients

	Univariate analysis			Multivariate analysis		
	No complication (n = 157, %)	Complication (n = 47, %)	P	OR	95%CI	P
Demographics						
Male	115 (73.2)	35 (74.5)	1.000			
Family history	6 (3.8)	2 (4.3)	1.000			
Smoking history	32 (20.4)	9 (19.1)	1.000			
Comorbidity	6 (3.8)	0 (0.0)	0.340			
Fistula-in-ano	73 (46.5)	17 (36.2)	0.243			
Previous abdominal surgery	10 (6.4)	8 (17.0)	0.037	3.61	1.23-10.60	0.020
Penetrating type	112 (71.3)	34 (72.3)	1.000			
Open approach	69 (43.9)	14 (70.2)	0.003	2.86	0.17-0.73	0.005
Preoperative medications						
Biologics	20 (12.7)	13 (27.7)	0.023	3.14	1.33-7.40	0.009
Steroid	24 (15.3)	13 (27.7)	0.082			
Immunomodulators	77 (49.0)	21 (44.7)	0.622			
Operation details						
Indications						
Fistula	53 (33.8)	20 (42.6)	0.300			
Obstruction	52 (33.1)	16 (34.0)	1.000			
Anastomosis configuration						
Side-to-side	126 (80.3)	37 (78.7)	0.837			
End-to-side	29 (18.5)	6 (12.8)	0.508			
Stapled anastomosis	155 (99.7)	46 (2.1)	0.546			
Additional procedures	45 (28.7)	21 (44.7)	0.050	1.38	0.61-3.14	0.444
Operation time ¹ > 135 min	52 (33.1)	25 (53.2)	0.016	2.38	1.17-4.84	0.017

¹Average operation time for CD was 135.6 min.

Results are reported as number (%). OR: Odds ratio; CI: Confidence interval.

complications[21,22]. Moreover, patients who had previous surgery were more inclined to develop postoperative complications ($P = 0.047$), particularly anastomotic leak ($P = 0.021$) and severe (Clavien-Dindo grade III/IV) complications ($P = 0.038$)[23]. A previous abdominal surgery history may result in prolonged dissection during surgery because of the atypical planes of disrupted normal anatomy, increasing the risks of accidental enterotomy and additional bowel devascularization[23].

In our study, the rate of conversion from laparoscopic to open surgery was about 5%. Pooled conversion rates have been found to range from 0% to 21.5%[13,24]. Recurrent disease with dense adhesions, pelvic sepsis with fistulizing disease, large inflammatory mass, and thickened mesentery are all conditions predisposing to conversion open surgery[24]. The low conversion rate in the present study may have been due to the relatively mild complexities and complications in patients who underwent laparoscopic surgery. Laparoscopy can be attempted in patients with CD, even if they have risk factors for open conversion. For safety reasons, however, patients should be converted to open surgery without delay.

Prevention of long-term postoperative recurrence in CD patients is a major challenge, especially as 10-15 year post-surgical recurrence rates are approximately 45% to 50%[25]. The long-term effects of laparoscopy have not been determined, as few studies have compared long-term outcomes, especially surgical recurrence, in CD patients who have undergone laparoscopic and open surgery. A meta-analysis

Table 5 Univariate and multivariate regression analyses of risk factors associated with surgical recurrence in propensity-score matched patients

	Univariate analysis			Multivariate analysis		
	No recurrence (n = 183)	Recurrence (n = 21)	P	HR	95%CI	P
Demographics						
Male	134 (73.2)	16 (76.2)	1.000			
Family history	8 (4.4)	0 (0.0)	1.000			
Smoking history	38 (20.8)	3 (14.3)	0.579			
Comorbidity	6 (3.3)	0 (0.0)	1.000			
Fistula-in-ano	81 (44.3)	9 (42.9)	1.000			
Previous abdominal surgery	15 (8.2)	3 (14.3)	0.407			
Penetrating type	129 (70.5)	17 (81.0)	0.445			
Open approach	95 (48.1)	14 (66.7)	0.166			
Preoperative medications						
Biologics	26 (14.2)	7 (33.3)	0.024	2.64	0.89-7.86	0.081
Steroid	31 (16.9)	6 (28.6)	0.229			
Immunomodulators	88 (48.1)	10 (47.6)	1.000			
Operation details						
Indication						
Fistula	69 (37.7)	4 (19.0)	0.099			
Obstruction	62 (33.9)	6 (28.6)	0.808			
Anastomosis configuration						
Side-to-side	150 (82.0)	13 (61.9)	0.042	3.82	1.24-11.78	0.078
End-to-side	30 (16.4)	5 (23.8)	0.370			
Stapled anastomosis	180 (98.4)	21 (100.0)	1.000			
Additional procedures	55 (30.1)	11 (52.4)	0.049	3.28	1.20-8.91	0.020
Operation time > 135 min	66 (36.1)	11 (52.4)	0.159			

Results are reported as number (%). HR: Hazard ratio; CI: Confidence interval.

reported that laparoscopic surgery is associated with a lower rate of late reoperations for CD recurrence (OR: 0.46; 95%CI: 0.27-0.80)[14], and laparoscopy was found to protect against surgical recurrence (HR: 0.24; 95%CI: 0.10-0.53; $P = 0.04$)[26]. Another study, however, reported no difference in surgical recurrence rates between surgical techniques (OR: 0.78; 95%CI: 0.54-1.11; $P = 0.17$)[27]. The present study also showed no difference in long-term outcomes between the LICR and OICR groups. Because this study was a retrospective analysis of a small number of patients, future large randomized-controlled trials are needed to assess the impact of laparoscopy on surgical recurrence.

Simultaneous surgery at the time of ICR was also associated with a higher risk of surgical recurrence. The extent of disease at diagnosis had an impact on recurrence, with higher recurrence rates in patients with small bowel and continuous ileocolonic CD than in patients with ileocecal and colorectal disease[28]. Disease extent > 50 cm is considered a risk factor for postoperative recurrence of CD[29]. An additional surgical procedure may be related to surgical recurrence because these patients may have more severe disease. Prospective clinical studies in larger numbers of patients are needed to further evaluate the results of the present study.

Since the introduction of the first anti-TNF agent in the late 1990s, biologic therapy has revolutionized the medical treatment of patients with CD[30]. Although administering biologics prior to surgery has been reported to reduce clinical/endoscopic recurrence rates[31-33], most of these trials had small sample sizes and limited follow-

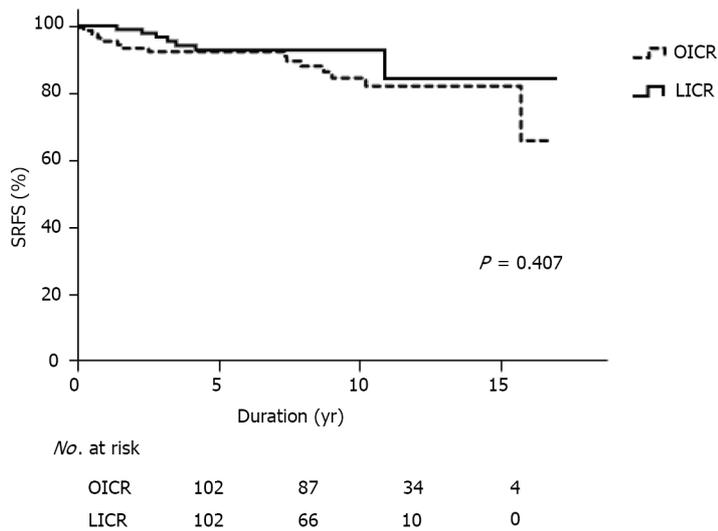


Figure 2 Kaplan-Meier analysis of surgical recurrence-free survival according to type of surgery in patients with Crohn's disease. SRFS: Surgical recurrence-free survival; LICR: Laparoscopic ileocolic resection; OICR: Open ileocolic resection.

up, and focused on endoscopic findings and clinical scores rather than repeat operations[30,34]. In our study, preoperative treatment with biologics was related to higher risk of surgical recurrence. South Korea strictly regulates the use of biologics due to health insurance policies, and prophylactic treatment with biologics is not available[35]. Therefore, the correlation between administration of biologics and higher risk of recurrence may be due to the greater severity of disease in patients selected for treatment with these agents. Large randomized-controlled trials are needed to determine the ability of routine prophylactic biologics after surgery to prevent surgical recurrence.

Stapled side-to-side anastomosis has been associated with lower rates of leakage and surgical recurrence than other types of anastomosis[36-39]. Side-to-side anastomoses maintain better lateral blood flow and a wide lumen, which prevents luminal stenosis and fecal pooling, thereby preventing early disease recurrence[40]. By contrast, another study reported that side-to-side anastomoses (both hand-sewn and stapled) did not reduce short-term complications and postoperative recurrence[41]. Moreover, anastomotic configuration or the material used was not significantly related to reoperations or complications[40]. The present study found that the type of anastomosis did not significantly affect short-term complications. Although the surgical recurrence rate tended to be higher in patients who underwent side-to-side than other types of anastomosis, the difference was not statistically significant (HR: 3.82; $P = 0.078$). However, most patients in the present study underwent side-to-side anastomosis, with only a few receiving end-to-side or end-to-end anastomosis. Surgeons in our center prefer side-to-side anastomosis in CD patients with extensive inflammation. Thus, to evaluate the role of anastomosis configuration, a more controlled study, adjusting for time period and surgeon, is needed.

The present study had several limitations. First, this study was a retrospective evaluation of patients at a single center. Randomized-controlled trials are required to specifically evaluate the ability of a laparoscopic approach to minimize postoperative complications. Although propensity-score matching can reduce selection bias, resulting in a situation similar to a randomized-controlled trial, our propensity-score matching models could not eliminate all selection biases. For example, the most frequent reasons for conversion to open surgery, such as adhesions and huge phlegmons, could not be calibrated by propensity-score matching analysis. Also, although the CDAI scores for both groups were moderate, the laparoscopic group had a significantly lower CDAI score (230.8) than the open group (269.1) ($P = 0.008$)[42]. Inevitably, a randomized controlled trial will be required to evaluate the role of the laparoscopic approach with more reliable evidence. Second, the study included only East Asian patients from a single country, thus not representing a global population. Korean and western CD patients differ in gender distribution, disease location, and perianal fistula occurrence[43]. Third, the use of biologics in this study was less frequent than in western studies because the health insurance reimbursement policy of the Korean government was strict during the study period. This study period was dominated by 'step-up treatment'. Although 'top-down treatment' has been more

frequent in recent years, its use in Korea is limited.

CONCLUSION

LICR yielded better short-term outcomes, including more rapid postoperative recovery, than open surgery. Long-term outcomes, however, did not differ between the two groups. Laparoscopic surgery might be a better surgical option in selected patients with CD.

ARTICLE HIGHLIGHTS

Research background

Ileocolic resection (ICR) is the most frequently performed operation for patients with abdominal Crohn's disease (CD) with involvement of the terminal ileum. Laparoscopic ICR (LICR) has become the preferred surgical approach for primary ileocolic CD because it has greater recovery benefits than open ICR (OICR).

Research motivation

The laparoscopic approach is regarded as more technically challenging than open surgery in CD patients with complex features, including huge phlegmons, multiple enteric fistulas, and dense adhesions, as well as those requiring repeated surgery. Utilization of LICR in patients with complex CD remains problematic.

Research objectives

This study aimed to compare the short- and long-term outcomes of LICR and OICR in patients with primary CD.

Research methods

A total of 348 eligible patients who underwent LICR or OICR for primary CD at Asan Medical Center in Seoul, Korea, from January 2006 to December 2017, were retrospectively analyzed. Data on demographic characteristics, preoperative disease characteristics, operative details, perioperative outcomes, and long-term surgical recurrence were collected. Patients were propensity-score matched 1:1 by factors potentially associated with 30 d perioperative morbidity.

Research results

During the study period, 348 patients underwent ICR, 211 by the open approach and 137 by the laparoscopic approach. Propensity-score matching yielded 102 pairs of patients. The rate of postoperative complications was significantly lower, postoperative hospital stay significantly shorter, and postoperative pain on day 7 significantly lower in patients who underwent laparoscopic than OICR. Surgical recurrence free survival (SRFS) rates in the OICR and LICR groups were not significantly different.

Research conclusions

LICR yielded better short-term outcomes and postoperative recovery than OICR, with no differences in long-term outcomes. LICR may provide greater benefits in selected patients with primary CD.

Research perspectives

The laparoscopic approach to ileocolic resection can be safely performed in patients with primary CD, resulting in fewer postoperative complications, faster postoperative recovery, and non-inferior surgical recurrence rate when compared with open surgery.

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