

Laparoscopic Versus Open Ileo-Colonic Resection in Crohn's Disease: Short- and Long-Term Results from a Prospective Longitudinal Study

Giuseppe S. Sica · Edoardo Iaculli ·
Domenico Benavoli · Livia Biancone ·
Emma Calabrese · Sara Onali · Achille L. Gaspari

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Abstract Possible relations between surgical approaches, frequency, and severity of Crohn's disease recurrence after ileo-colonic resection is unknown. We aimed to assess perioperative outcomes and postsurgical complications of laparoscopic versus standard open surgery and to detect differences between the two groups in endoscopical recurrence and patients' satisfaction. Twenty-eight consecutive patients undergoing elective ileo-colonic resection by either laparoscopic approach ($n=15$) or conventional open surgery ($n=13$) were prospectively enrolled. No mortality or major intraoperative complications were observed in both groups. Significant differences between groups were the median operating time found shorter in the open group than in the laparoscopic group ($p=0.003$), the higher dosage of pain killers needed in the open group ($p=0.05$), the passage of flatus and/or stool after surgery found faster in group A ($p=0.004$) and the shorter recovery period in the laparoscopic group ($p=0.007$). Colonoscopy was performed in 27 patients. The frequency and pattern of recurrence did not differ between the two groups ($p=0.63$). Patients' satisfaction was significantly in favor of laparoscopy. Present findings support the feasibility and advantages in the short-term of laparoscopic ileo-colonic resection in patients with Crohn's disease. No differences were observed in terms of frequency, time of onset, and severity of recurrence in a 1-year follow-up.

Keywords Crohn's disease surgery · Laparoscopic surgery · Recurrence · Quality of life

Introduction

Laparoscopic (lap) ileo-cecal resection has been proposed with increasing interest in surgical treatment of Crohn's disease (CD).¹ As CD is a benign disease, laparoscopic treatment is not ethically questionable. However, long-

standing inflammation and physiopathologic characteristics of the disease may determine the procedure long, tricky, or even hazardous.^{2–4}

It is clear that laparoscopic approach to surgery in CD can be proposed only after its feasibility and effectiveness is demonstrated. Furthermore, prospective and randomized trials, analyzing significant short- or long-term clinical benefits, may indicate laparoscopy as the procedure of choice for ileo-colonic resection in CD.

A correlation between clinical outcome of CD patients after laparoscopy^{5–10} and host immune response^{11–15} has been postulated, although statements at this regard are not conclusive. Although recurrence of the lesions is an almost ineluctable event in CD,^{16,17} possible relations between surgical approaches, frequency, and severity of recurrence after ileo-colonic resection is unknown.

On the basis of these observations and as the role of laparoscopy in CD is still undefined, in a prospective nonrandomized longitudinal study, we compared the short- and long-term outcome of CD patients undergoing ileo-colonic resection by using a laparoscopic or laparotomic approach and followed up for 1 year.

G. S. Sica (✉) · E. Iaculli · D. Benavoli · A. L. Gaspari
Dipartimento di Chirurgia, Unità di Chirurgia Generale,
Università di "Tor Vergata",
Viale Oxford 81,
00133 Rome, Italy
e-mail: sica.giuseppe@fastwebnet.it

L. Biancone · E. Calabrese · S. Onali
Dipartimento di Medicina, Unità di Gastroenterologia,
Università di "Tor Vergata",
Viale Oxford 81,
00133 Rome, Italy

The primary end point of the study was to assess the perioperative outcomes and postsurgical complications of laparoscopic surgery versus standard open surgery in a consecutive nonselected series of patients in regular follow-up in a referral Inflammatory Bowel Disease (IBD) center undergoing ileo-colonic resection in a single surgical unit. Differences between the two groups in terms of time free from clinical and endoscopical relapse, including frequency severity and prevalent pattern of postoperative recurrence were investigated. At this purpose, clinical activity was assessed every 3 months for 1 year and finding compatible with endoscopical recurrence searched at 1 year. Patients' satisfaction regarding the surgical procedure was also recorded and a specific questionnaire fulfilled.

Materials and Methods

Patients

In a prospective nonrandomized longitudinal study, 28 consecutive patients undergoing elective resection for ileo-colonic CD from October 2004 to June 2005 at the gastrointestinal (GI) surgical unit of the University "Tor Vergata" of Rome were prospectively enrolled. All patients were in regular follow-up at the referral IBD center of the same university hospital. In all patients, the diagnosis of CD was assessed according to conventional clinical, endoscopical, histological and radiological criteria. No absolute specific contra-indications to laparoscopic ileo-colonic resection are indeed reported in CD patients. Inclusion criteria were: (1) regular follow-up at the GI unit of the University "Tor Vergata" of Rome, Italy; (2) indication for elective ileo-

colonic resection for CD related to complications, refractory or steroid-dependent disease; (4) resection performed at the GI surgical unit of the University "Tor Vergata" of Rome, Italy; (5) agreement to follow the study protocol; (6) written informed consent. Exclusion criteria included (1) age <15 or >65, (2) BMI >30; (3) emergency surgery.

Demographic and clinical characteristics of the 28 patients are summarized in Table 1. As shown, there were 14 men and 14 women, with a median age of 33 years (range, 16–64) and a median disease duration of 4 years (range, 0–38). Indication for surgery was symptomatic ileal stenosis in most of the patients (79%), followed by abdominal abscess (25%), entero-enteric or entero-cutaneous fistula (14%) and medical therapy failure (steroid-dependence) in one patient (4%; Table 2). Most of the 28 patients had more than one single complication. Treatment at time of surgical indication included oral corticosteroids (68%), mesalazine (43%), antibiotics (43%), and azathioprine (21%; concomitant drug treatments in most of the patients).

Surgical Treatment

Enrolled patients underwent elective ileo-colonic resection by either laparoscopic approach (group A, LAP; $n=15$) or conventional open surgery (group B, OPEN; $n=13$; Table 1). Both surgical approaches were performed by experienced GI surgeons. This is a nonrandomized study, however, surgical approach was not selected on the basis of clinical and anatomopathological characteristics of the disease (as demonstrated by homogeneous incidence of fistula and abscess in the two groups; Table 1), but the only bias was the availability of a surgeon with advanced

Table 1 Demographics and Clinical Characteristics of CD Patients Undergoing Laparoscopic (Group A) or Laparotomic (Group B) Ileo-Colonic Resection

	Group A Laparoscopy ($n=15$)	Group B Laparotomy ($n=13$)	p Value (>0.05 ns)
Age median (range), years	32 (16–45)	36 (24–64)	0.06
Gender (M/F)	7/8	7/6	
BMI median (range), kg/m	22 (19.7–29.4)	23 (18–28.4)	0.65
CD duration median (range), years	3 (0–16)	4 (0–38)	0.18
CD site	12 I; 3 I–C	12 I; 1 I–C	
Pre-operative treatment n patients (%) ^a			
Azathioprine (2–2.5 mg/kg)	2 (13%)	4 (30%)	0.37
Corticosteroids (from 1 mg/kg)	12 (80%)	7 (54%)	0.22
Mesalazine (2.4 g/day)	5 (33%)	7 (54%)	0.44
Antibiotics (ciprofloxacin, metronidazole)	5 (33%)	7 (54%)	0.44
Disease complications(%) ^b			
Stenosis	14 (93%)	9 (69%)	0.15
Entero-enteric fistulae	8 (53%)	8 (62%)	0.71
Intra-abdominal abscess	3 (20%)	4 (31%)	0.67
Entero-cutaneous fistula	0	1 (8%)	0.46
Extraintestinal involvement (uveitis)	1 (7%)	0	Ns

I Ileum, I–C ileum-colon

^a Sixty percent of the patients in group A and 62% in group B received ≥ 2 concomitant treatments for CD.

^b Seventy-three percent of the patients in group A and 62% in group B showed ≥ 1 complication.

Table 2 Perioperative Outcome

	Group A Laparoscopy (n=15)	Group B Laparotomy (n=13)	<i>p</i> Value (>0.05 ns)
Indication for surgery, <i>n</i> patients (%) ^a			
Medical therapy failure	0	1 (8%)	0.46
Stricture with partial obstruction	14 (93%)	8 (62%)	0.06
Enteroenteric/enterocutaneous fistula	1 (7%)	2/1 (23%)	0.31
Intra-abdominal abscess	3 (20%)	4 (31%)	0.67
Length of resected bowel			
Median (range), cm	110 (70–130)	102.5 (45–160)	0.46
Anastomosis (side to side/end to side)	15/0	13/0	
Duration of surgical procedure			
Median (range), min	185 (120–240)	140 (100–220)	0.003
Intraoperative complications, <i>n</i> patients (%)			
Intraoperative bleeding	0	0	
Intraoperative blood transfusion	1	1	Ns
Postoperative blood transfusion	3 (20%)	2 (15%)	Ns
Conversion	2 (13%)		
Adjunctive procedures, <i>n</i> patients (%)			
Additional small bowel resection	4	1	
Rectal segmentary resection	1	1	
Colecistectomy	1	1	
Meckel diverticulectomy	2	0	
Fistula suture	1	4	
Fimbrioplasty	1	0	

^a Some patients had more than one indication for surgery.

training in GI laparoscopic surgery. Laparoscopy was converted to laparotomy according to surgeon's judgment during surgical resection.

A three-port approach was used for the laparoscopic procedures. All three trocars were 10–12 mm and placed infra-umbilical, suprapubic, and in left iliac fossa; in case an intra-abdominal anastomosis was performed, an additional 5 mm trocar was placed in epigastrium. The mesentery was divided using radiofrequency scalpel (Ligasure LS® 110, Valleylab) and eventually stapled or oversewn if particularly thick. The anastomosis was performed either mechanically or manually in a side-to-side fashion. The laparoscopic approach was considered successful whenever it was possible to complete the entire intestinal resection. One of the port incision was extended up to 4 cm to extract the resected intestine and eventually used to fashion the anastomosis. The procedure was to be converted to open surgery if the time of dissection was superior of 90 min. Converted laparoscopic cases were analyzed on an intention-to-treat basis.

The open ileo-colonic resection was formally the same as the laparoscopic technique, but it required a midline laparotomy (15 cm±3).

In both groups, the same postoperative protocol was used. Patients were allowed to oral intake when there was return of bowel function. All patients were discharged from the hospital when in general well-being and able to return to daily activity. Fast track protocol was not used in any patient.

Study Protocol

In a prospective longitudinal study, recurrence was assessed 1 year after ileo-colonic resection, using ileocolonoscopy as gold standard. The degree of recurrence and the prevalent pattern of the lesions was assessed by one single endoscopist, according to Rutgeerts et al.,¹⁶ on a 0 to 4 score, as previously reported.²³

To detect possible early asymptomatic postoperative recurrence requiring more aggressive treatment and to assess the possible role of noninvasive techniques for detecting CD recurrence, a subgroup of ten compliant patients were also studied at 3, 6, and 12 months by small intestine contrast ultrasonography (SICUS) and wireless capsule endoscopy (WCE). SICUS was performed after 375 ml (range, 250–500 ml) polyethilen glycole (PEG; Promefarm, Milano, Italy) ingestion. WCE was performed by using the given M2A capsule.^{18–25} WCE was not performed in patients showing by SICUS or colonoscopy findings compatible with strictures, in relation to the impact risk. In all patients, clinical activity of CD was assessed at 12 months according to the Crohn's disease activity index (CDAI).²⁶ All patients were treated with mesalazine (2.4 g/day) within 1 month from surgery for 1 year.

At 12 months, patients were also asked to fill a specific treatment-satisfaction questionnaire modified from Dunker's et al. Hospital Experience Questionnaire²⁷ (Fig. 1).

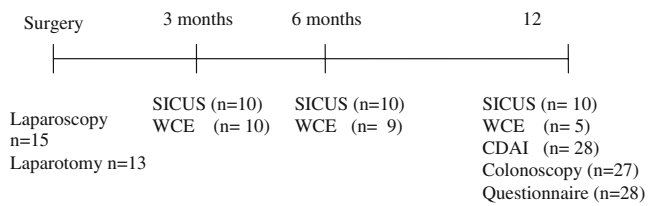


Figure 1 Follow-up schedule of enrolled patients. As shown, ileo-colonic resection was performed using a laparoscopic approach in 15 patients and a laparotomic approach in 13 patients.

Statistical Analysis

Parameters analyzed as confounding criteria are indicated in Table 1. Tables 2 and 3 show the confounding criteria considered for the assessment of the peri- and postoperative period. All data were collected on a Microsoft® Excel spreadsheet. Results were expressed as median and range of observed values. Qualitative data were statistically compared using Fisher's exact test; quantitative data showing normal distribution were compared using a paired *t* test. Regardless of the statistical analysis used, a *p*<0.05 value was considered statistically significant.

Results

Patients

Among the whole group of 28 patients, 15 underwent laparoscopic (LAP; group A) and 13 had an open (OPEN; group B) ileo-colonic resection. Two laparoscopic procedures were converted to laparotomy after a trial dissection (conversion rate, 13.3%) because of an extremely friable mesenter related to the presence of enteric fistulas and abscesses in one patient and of a large inflammatory mass occupying most of the pelvis in the second patient. In these two cases, data were collected and analyzed on an intention-to-treat basis.

In all patients, histologic analysis of the resected bowel tissue confirmed the diagnosis of CD involving the distal ileum, including also the cecum or the right colon in four patients.

Table 1 shows demographics and clinical characteristics of CD patients undergoing LAP (group A) or OPEN (group B) ileo-colonic resection. As shown, there are no significant differences between the two groups.

Table 3 Clinical Outcome After Surgery

	Group A Laparoscopy (n=15)	Group B Laparotomy (n=13)	<i>p</i> Value (>0.05 ns)
Length of hospital stay median (range), days	7 (5–10)	7 (6–28)	0.14 ns
Passage of flatus median (range), days	3 (2–4)	4 (3–8)	0.004
Analgesic requirement median (range), days	5 (3–8)	5 (3–8)	0.35 ns
Analgesic requirement median (range), doses	7 (3–17)	11 (4–21)	0.05
Opioid (100 mg tramadol or 10 mg morphine)	2 (1–4)	2 (1–8)	0.09 ns
Non-opioid (30 mg ketorolac)	5 (0–16)	6 (0–16)	0.35 ns
Tolerance to solid diet median (range), days	6 (4–7)	6 (4–26)	0.17 ns
Return to normal activity (sport/work) median (range), days	40 (30–90)	70 (35–150)	0.007
Complications within 30 days			
n patients (days to recover)	2	2	Ns
Abdominal abscess		1 (20)	0.46
Surgical wound infection	2 (10/14)	1 (20)	Ns
Complications in the long term (1 year)			
Adhesions/ileus	0	0	
Incisional hernia	0	0	
Clinical and endoscopic follow-up (1 year)			
Symptomatic recurrence (CDAI>150)	0/15 (0%)	0/13 (0%)	Ns
Endoscopic recurrence	13/14 (93%)	13/13 (100%)	
Rutgeert's score, median (range)	3 (0–4)	3 (1–4)	0.63 ns

Perioperative Clinical Outcomes

There were no major intraoperative complications in both groups. Perioperative results are summarized in Table 2. Surgical resection was successfully completed laparoscopically in all but two patients in group A (87%). The only significant difference between groups was the median operating time found shorter in the OPEN group (140 min; range, 100–220) than in the LAP group (185 min; range, 120–240; $p=0.003$).

Short- and Long-Term Outcome

Significant differences between groups A and B were found analyzing the short-term outcome as outlined in Table 3. Pain after surgery was evaluated on analgesic requirement basis, and the dosage of pain killers administered per patient was significantly higher in the OPEN group (median and range in LAP versus OPEN: 7 doses (range 3–17) versus 11 doses (range 4–21); $p = 0.05$). Passage of flatus and/or stool after surgery was faster in group A than in group B (LAP versus OPEN: median 3 days (range 2–4) versus median 4 days (range 3–8); $p = 0.004$). Similarly, there was a statistically significant shorter recovery period (time between hospital discharge and return to normal activities and work) in the laparoscopic group: LAP median 40 days (range 30–90) versus OPEN median 70 days (range 35–150; $p=0.007$).

Frequency of postoperative complications at 30 days was comparable between the two groups. Two patients from the LAP group showed superficial infection of the surgical incision that required, respectively, 10 and 14 days of outpatient medications. One patient in the OPEN series had an abdominal abscess possibly caused by a small anastomotic leakage that completely healed after a CT-guided drainage of the abscess cavity and 20 days of total parenteral nutrition. The second patient in the open group had an abscess at the site of surgical incision that required a 6-day admission at the GI unit, surgical drainage, and wound toilette, followed by complete healing within 20 days of outpatient medications.

No long-term (1 year) surgery-related complications, including death, strictures, adhesions ileus/symptoms, or incisional hernias were observed in the two groups, and no patients required any additional surgical treatment related to CD at 1 year. Among the 14 females enrolled, 3 from the LAP group became pregnant after surgery (Fig. 1).

Clinical and Endoscopical Recurrence

The frequency and severity of recurrence in patients resected using a laparoscopic or laparotomic approach was

investigated in a 1-year follow-up. All 28 patients completed the clinical follow-up at 1 year and maintained the clinical remission ($CDAI < 150$) while on mesalazine (2.4 gr/day). Among the 10 compliant patients also studied by non-invasive techniques, SICUS showed lesions compatible with recurrence in four out of ten patients at 3 months, in eight out of ten patients at 6 months, and in all the ten patients at 12 months. WCE detected findings compatible with CD recurrence in nine out of ten patients at 3 months, in eight out of nine patients at 6 months (one patient did not perform WCE because of a high-impact risk related to lumen narrowing detected by SICUS), and in four out of five patients at 12 months (five patients did not perform WCE because of lumen narrowing detected by SICUS or colonoscopy).

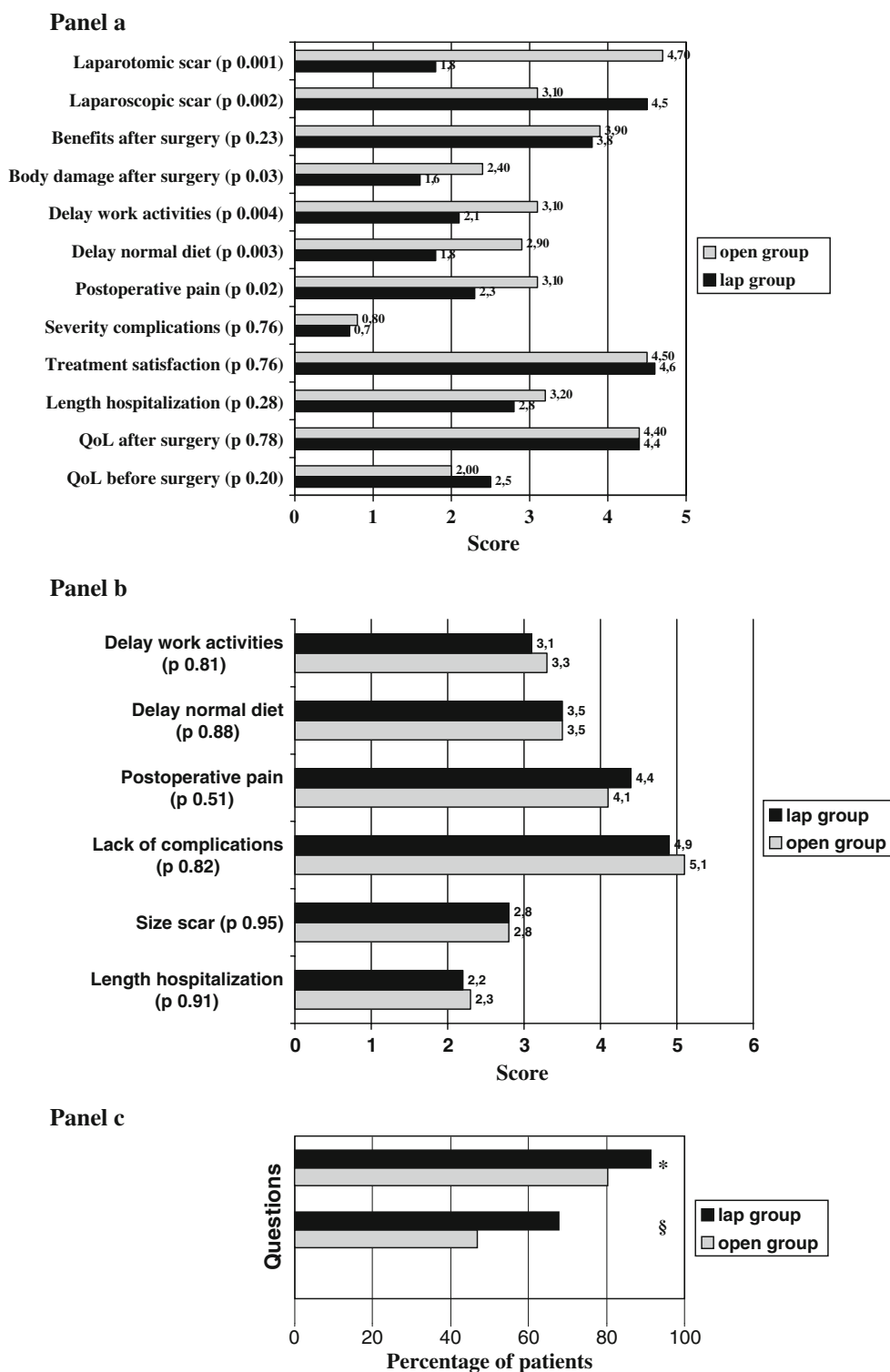
Ileocolonoscopy represented the gold standard for assessing CD recurrence at 1 year. Among the 28 patients completing the clinical follow-up, ileocolonoscopy was performed in 27, as 1 asymptomatic patient was already clearly pregnant at the time. Endoscopic recurrence was, therefore, assessed in 14 patients from the LAP and in 13 patients from the OPEN group. Results are shown in Table 3. Among the whole group of 27 patients assessed by ileocolonoscopy, recurrence was detected in 26 (96.2%). The frequency of recurrence was, therefore, comparable between the two groups (LAP, 13 out of 14, 92.8%, versus OPEN, 13 out of 13, 100%). The median endoscopic score of recurrence in the whole group of 27 patients was 3 (range, 0–4) and did not significantly differ between the two groups (LAP versus OPEN: median 3, range 0–4, versus median 3, range 1–4; $p=0.63$). The prevalent pattern of CD lesions (fistulizing, fibrostricturing, or inflammatory) assessed by endoscopy at 1 year was also comparable in the two groups (LAP group: 2 fibrostricturing, 12 inflammatory; OPEN group: 1 fibrostricturing, 12 inflammatory). The presence of fibrostricturing recurrence not allowing passage of the endoscope (grade 4 recurrence with stenosis) was observed in two patients from the LAP group and in one patient from the OPEN group. The recurrence involved the perianastomotic area (including the neoterminal ileum only and/or the anastomosis) in all patients from both the LAP and OPEN group, as it is in most cases. In particular, among the 13 CD patients from the LAP group showing recurrence, recurrent lesions involved both the anastomosis and the neoterminal ileum in six patients, only the neoterminal ileum in three patients, and only the anastomosis in four patients. Among the 13 patients with endoscopic recurrence at 1 year from the OPEN group, lesions involved both the neoterminal ileum and the anastomosis in the 12 and only the neoterminal ileum in the remaining patient, whereas no patient showed lesions involving the anastomosis only.

Treatment Satisfaction Questionnaire

Patients also filled out the specific treatment satisfaction questionnaire (TSQ)²⁷ to evaluate differences between the two surgical techniques in subjective outcomes and in “treatment’s compliance according to patient expectation.”

Figure 2 a–c Histograms showing results from the treatment satisfaction questionnaire (TSQ) in patients with ileocolonic resection performed using a laparoscopic or laparotomic approach. **a** Results from TSQ. **b** Patient’s perception of the most relevant aspect of the treatment. **c** Asterisk Percentage of patients in both groups that ideally would prefer the laparoscopic approach in case of a second operation and *section sign* are willing to pay for having a laparoscopic operation

Figure 2a–c shows the results from the TSQ (patients with converted LAP procedure were considered part of group B–OPEN). As shown, patients’ satisfaction regarding the surgical scar, the body damage after surgery, delay of work activity, delay of normal diet, postoperative pain, and length of hospitalization was significantly in favor of laparoscopy than laparotomy (Fig. 2).



The other parameters considered did not significantly differ between patients resected using the laparoscopic versus the laparotomic approach (Fig. 2a–c).

Discussion

Laparoscopic surgery in CD patients is attractive and promising (minimal scars, less adhesions, faster recovery) but also challenging and controversial.

To assess feasibility and efficacy of laparoscopic ileo-colonic resection, we designed a prospective nonrandomized longitudinal study that assigned a patient to laparoscopic or laparotomic surgical resection on the basis of the casual availability the day of surgery of an expert GI laparoscopic surgeon. All the enrolled patients were in regular follow-up at the same referral IBD unit. In our CD population, the two comparative groups were comparable in terms of demographics and clinical characteristics at baseline. Apart from age and emergency surgery, morbid obesity was the only exclusion criteria used, and these patients were not included in the study protocol. However, a BMI > 30 is observed in a small subgroup of patients in our IBD referral center.

Therefore, present findings allow an appropriate comparison in terms of short- and long-term postsurgical outcome between patients with ileo-colonic resection performed by using two different surgical approaches.

By our knowledge, only two randomized studies compared the outcome of laparoscopic and laparotomic ileo-cecal resection for CD. The study from the Cleveland Clinic randomized preselected CD patients after a diagnostic laparoscopy that basically allowed surgeons to select a subgroup of patients with more favorable disease.²⁸ Differently, in the Dutch study, the procedure was only laparoscopic assisted, as the major part of the operation was a standard open procedure. In fact, both the intestine and the mesentery with its vessels were divided through the mini-laparotomy, and all the anastomoses were manually fashioned after the open resection was completed.²⁹

The main purpose of the present study was to demonstrate the feasibility of the minimally invasive approach in the majority of patients undergoing elective ileo-colonic resection for CD. Although present findings are preliminary and the number of patients is small to draw conclusive statements at this regard, the conversion rate was very low (13%), being comparable to other studies.³⁰ This finding was observed in spite of the high frequency of fistulizing disease and presence of abscesses at time of surgery. No mortality or morbidity was observed in our study population, thus being comparable between the 2 groups.

Present findings from a prospective longitudinal study, using as only criterion the availability of an expert laparoscopic surgeon for choosing the surgical approach,

strongly suggest that it is feasible, safe, and ethically acceptable to blindly randomize CD patients undergoing elective ileo-colonic resection to a laparoscopic or laparotomic surgery. Present findings suggest a better postsurgical outcome in patients resected according to a laparoscopic approach when considering recovery of bowel functions, doses of analgesics required, and recovery to normal activities ($p=0.004$, 0.05 , and 0.007 , respectively). Moreover, as the outcome of surgery in CD patients appear not to be worsened after laparoscopic surgery, our findings confirm that laparoscopic ileo-colonic resection is equivalent to the standard procedure in terms of “curative” resection of all the affected bowel, and of treatment of complications (i.e., abscesses, fistulae).

Beside the already known advantages of laparoscopy,^{30–33} its use in CD may play a major role in this particular population of patients, often requiring surgery at young age. The psychological impact of a less invasive surgical approach, associated with a smaller scar, earlier recovery, and return to daily activities, may represent a relevant issue in CD population. On the basis of the results from the present study, enrollment of new patients and longer follow-up studies are ongoing in our IBD unit to assess the potential long-term benefits of laparoscopic surgery (e.g., adhesions, recurrence, hernias) in CD.^{33,34} The specific IBD QoL questionnaire SF-36 and GIQLI are not appropriate to evaluate the differences between the two surgical techniques. We, therefore, used a modified version of the TSQ questionnaire previously proposed by Dunker et al.,²⁷ useful to focus on body-image satisfaction and hospital-staying experience, also considering possible reinterventions. In our study, treatment’s satisfaction assessment showed a high acceptance of surgical treatment in both groups, being considered useful and beneficial. Laparoscopy showed advantages in terms of cosmesis and postoperative subjective experience during hospitalization and recovery. In addition, 92% of patients from the laparoscopic group and 80% of patients from the laparotomic group referred to hypothetically prefer the mini-invasive laparoscopic approach in the eventuality of a subsequent surgical treatment.

Additional aim of the present study was to address whether a laparoscopic versus a laparotomic surgical approach may influence the clinical outcome and the frequency and prevalent pattern of the lesions assessed by colonoscopy 1 year after surgery. As a matter of fact, although the etiology of CD remains unknown, current evidences indicate that a genetically inappropriate host immune response toward luminal antigens, particularly the common bacterial flora, plays a major role in the pathogenesis of the disease.^{35–41} Whether a laparoscopic versus a laparotomic approach may influence the host immune response has been investigated in both benign and malignant diseases.^{35,36} Despite the large number of

studies, little is still known about possible clinical implications of these immunologic aspects in CD, and no studies investigated the possible influence of laparoscopy on the frequency and severity of CD recurrence.⁴² Results from our prospective longitudinal study assessing the clinical and endoscopic outcome in an homogeneous cohort of CD patients undergoing elective laparoscopic or open ileo-colonic resection failed to support differences in terms of both clinical relapse and of frequency and severity of endoscopic recurrence at 1 year in the two groups. In our series, all patients resected by using either a laparoscopic or laparotomic approach indeed maintained clinical remission 1 year after surgery. The frequency of recurrence was also observed in a comparable proportion of patients from both groups. In fact, all enrolled patients but one developed asymptomatic endoscopic recurrence at 1 year. The prevalent pattern of the lesions at 1 year was also comparable in the two groups.

Our occasional finding that three out of the eight females became pregnant after laparoscopic surgical resection further supports a favorable clinical outcome of laparoscopic surgery. Possible differences in terms of clinical outcome in relation to the surgical approach are under investigation in this cohort of patients, as a longer follow-up period may be required. At this purpose, new and promising noninvasive diagnostic techniques such as SICUS and WCE may be useful for future studies aimed to investigate the natural history of CD recurrence after ileo-colonic resection.

Conclusion

Present findings support the feasibility of laparoscopic ileo-colonic resection in a nonselected consecutive series of CD patients. We confirmed the well-known advantages in the short-term (postoperative recovery) and safety of this technique. Results from the present study also indicate a significant preference of patients for the mini-invasive approach because of its cosmetic results, hospital experience, and surgical treatment acceptance.

On the other hand, in our CD population, no differences were observed in terms of frequency, time of onset, and severity of clinical and endoscopic recurrence in a 1-year follow-up. Long-term results, including frequency of adhesions, hernias, and reoperations, are under investigation in a larger population of patients and require a longer follow-up.

References

- Ludwig K, Milsom JW, Church JM, Fazio VW. Preliminary experience with laparoscopic intestinal surgery for Crohn's disease. *Am J Surg*. 1996;171:52–56.
- Wu JS, Birnbaum EH, Kodner IJ, Fry RD, Read TE, Fleshman JW. Laparoscopic-assisted ileocolic resections in patients with Crohn's disease: are abscesses, phlegmons, or recurrent disease contraindications? *Surgery*. 1997;122:682–689.
- Watanabe M, Hasegawa H, Yamamoto S, Hibi T, Kitajima M. Successful application of laparoscopic surgery to the treatment of Crohn's disease with fistulas. *Dis Colon Rectum*. 2002;45(8):1057–1061.
- Hasegawa H, Watanabe M, Nishibori H, Okabayashi K, Hibi T, Kitajima M. Laparoscopic surgery for recurrent Crohn's disease. *Br J Surg*. 2003;8:970–973.
- Gupta A, Watson DI. Effect of laparoscopy on immune function. *Br J Surg*. 2002;10:1296–1306.
- Balagué C, Taragoma EM, Pujol M, Filella X, Espert JJ, Trias M. Peritoneal response to a septic challenge. Comparison between open laparotomy, pneumoperitoneum laparoscopy, and wall lift laparoscopy. *Surg Endosc*. 1999;13:792–796.
- West MA, Hackam DJ, Baker J, Rodriguez JL, Bellingham J, Rotstein OD. Mechanism of decreased in vitro murine macrophage cytokine release after exposure to carbon dioxide: relevance to laparoscopic surgery. *Ann Surg*. 1996;226:179–190.
- Gutt CN, Heinz P, Kaps W, Paolucci V. The phagocytosis activity during conventional and laparoscopic operations in the rat: a preliminary study. *Surg Endosc*. 1997;11:899–901.
- Chekan EG, Nataraj C, Clary EM, Hayward TZ, Brody FJ, Stamat JC, Fina MC, Eubanks WS, Westcott CJ. Intraperitoneal immunity and pneumoperitoneum. *Surg Endosc*. 1999;13:1135–1138.
- Schietroma M, Carlei F, Lezoche E, Agnelli A, Enang GN, Mattucci S, Minervini S, Lygidakis NJ. Evaluation of immune response in patients after open or laparoscopic cholecystectomy. *Hepatogastroenterology*. 2001;48:642–646.
- Ina K, Binion DG, West GA, Dobrea GM, Fiocchi C. Crohn's disease (CD) mucosal T-cells are resistant to apoptosis (abstract). *Gastroenterology*. 1995;108:A841.
- Mayer L, Eisenhardt D. Lack of induction of suppressor T cells by intestinal epithelial cells from patients with inflammatory bowel disease. *J Clin Invest*. 1990;86:1255–1260.
- Kusugami K, Youngman KR, West GA, Fiocchi C. Intestinal immune reactivity to interleukin 2 differs among Crohn's disease, ulcerative colitis and control. *Gastroenterology*. 1989;97:1–7.
- James SP. Remission of Crohn's disease after human immunodeficiency virus infection. *Gastroenterology*. 1998;95:1667–1669.
- Plevy SE, Landers CJ, Prehn J, Carramanzana NM, Deem RL, Shealy D, Targan SR. A role for TNF-alpha and mucosal T helper-1 cytokines in the pathogenesis of Crohn's disease. *J Immunol*. 1997;159(12):6276–6282.
- Rutgeerts P, Geboes K, Vantrappen G, et al. Predictability of the postoperative course of Crohn's disease. *Gastroenterology*. 1990;99:956–963.
- Pallone F, Boirivant M, Stazi MA, et al. Analysis of clinical course for postoperative recurrence of Crohn's disease. *Gastroenterology*. 1983;85:917–921.
- Parente F, Greco S, Molteni M, Anderloni A, Sampietro GM, Danelli PG, Bianco R, Gallus S, Bianchi Porro G. Oral contrast enhanced bowel ultrasonography in the assessment of small intestine. Crohn's disease A prospective comparison with conventional ultrasound, x ray studies and ileocolonoscopy. *Gut*. 2004;53(11):1652–1657.
- Triester SL, Leighton JA, Leontiadis GI, Gurudu SR, Fleischer DE, Hara AK, Heigh RI, Shiff AD, Sharma VK. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease. *Am J Gastroenterology*. 2006;101(5):954–964.
- Calabrese E, La Seta F, Buccellato A, Virdone R, Pallotta N, Corazziari E, Cottone M. Crohn's disease: a comparative prospective study of transabdominal ultrasonography, small

- intestine contrast ultrasonography, and small bowel enema. *Inflamm Bowel Dis*. 2005;11(2):139–145.
21. Spada C, Spera G, Riccioni M, Biancone L, Petruzzello L, Trincali A, Familiari P, Marchese M, Onder G, Mutignani M, Perri V, Petruzzello C, Pallone F, Costamagna G. A novel diagnostic tool for detecting functional patency of the small bowel: the given patency capsule. *Endoscopy*. 2005;37(9):793–800.
 22. Biancone L, Calabrese E, Petruzzello C, Onali S, Caruso A, Palmieri G, Sica G, Pallone F. Wireless capsule endoscopy and small intestine contrast ultrasonography in recurrence of Crohn's disease. *Inflamm Bowel Dis*. 2007;13(10):1256–1265.
 23. Biancone L, Fiori R, Tosti C, Marinetti A, Catarinacci M, De Nigris F, Simonetti G, Pallone F. Virtual colonoscopy compared with conventional colonoscopy for stricturing postoperative recurrence in Crohn's disease. *Inflamm Bowel Dis*. 2003;9(6):343–350.
 24. Iddan G, Meron G, Glukhovskiy A, et al. Wireless capsule endoscopy. *Nature*. 2000;405:417.
 25. Triester SL, Leighton JA, Leontiadis GI, Gurudu SR, Fleischer DE, Hara AK, Heigh RI, Shiff AD, Sharma VK. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease. *Am J Gastroenterol*. 2006;101(5):954–964.
 26. Best W, Bechtel JM, Singleton JW, et al. Development of a Crohn's disease activity index. *Gastroenterology*. 1976;70:439–444.
 27. Dunker MS, Stiggelbout AM, van Hogezaand RA, Ringers J, Griffioen G, Bemelman WA. Cosmesis and body image after laparoscopic-assisted and open ileocolic resection for Crohn's disease. *Surg Endosc*. 1998;12:1334–1340.
 28. Milsom JW, Hammerhofer KA, Bohm B, Marcello P, Elson P, Fazio VW. Prospective randomized trial comparing laparoscopic vs conventional surgery for refractory ileocolic Crohn's disease. *Dis Colon Rectum*. 2001;44:1–9.
 29. Maartense S, Dunker MS, Slors JF, Cuesta MA, Pierik EG, Gouma DJ, Hommes DW, Sprangers MA, Bemelman WA. Laparoscopic-assisted versus open ileocolic resection for Crohn's disease: a randomized trial. *Ann Surg*. 2006;243(2):143–149. (discussion 150–3).
 30. Tilney HS, Constantinides VA, Heriot AG, Nicolau M, Athanasiou T, Ziprin P, Darzi AW, Tekkis PP. Comparison of laparoscopic and open ileocecal resection for Crohn's disease: a meta-analysis. *Surg Endosc*. 2006;20:1036–1044.
 31. Shore G, Gonzalez QH, Bondora A, Vickers SM. Laparoscopic vs conventional ileocelectomy for primary Crohn disease. *Arch Surg*. 2003;138:76–79.
 32. Young-Fadok TM, Hall Long K, McConnel EJ, Gomez Rey G, Cabanela RL. Advantages of laparoscopic resection for ileocolic Crohn's disease: improved outcomes and reduced costs. *Surg Endosc*. 2001;15:450–454.
 33. Bergamaschi R, Pessaix P, Arnaud JP. Comparison of conventional and laparoscopic ileocolic resection for Crohn's disease. *Dis Colon Rectum*. 2003;46:1129–1133.
 34. Majewski WD. Long-term outcome, adhesions, and quality of life after laparoscopic and open surgical therapies for acute abdomen. *Surg Endosc*. 2005;19:81–90.
 35. Wu FP, Cuesta MA, Sietses C. Randomized clinical trial of the effect of open versus laparoscopically assisted colectomy on systemic immunity in patients with colorectal cancer. *Br J Surg*. 2001;88:801–807.
 36. Buunen M, Gholghesaei M, Veldkamp R, Meijer DW, Bonjer HJ, Bouvy ND. Stress response to laparoscopic surgery. *Surg Endosc*. 2004;18:1022–1024.
 37. Fiocchi C. Inflammatory bowel disease: etiology and pathogenesis. *Gastroenterology*. 1995;115:182–205.
 38. Monteleone I, Vavassori P, Biancone L, Monteleone G, Pallone F. Immunoregulation in the gut: success and failures in human disease. *Gut*. 2002;50(Suppl 3):III60–III64.
 39. Pallone F, Fais S, Squarcia O, Biancone L, Pozzilli P, Boirivant M. Activation of peripheral blood and intestinal lamina propria lymphocytes in Crohn's disease. "In vivo" state of activation and "in vitro" response to stimulation as defined by the expression of early activation antigens. *Gut*. 1987;28:745–753.
 40. Monteleone G, Biancone L, Marasco R, Morrone G, Marasco O, Luzzza F, Pallone F. Interleukin-12 (IL-12) is expressed and actively released by Crohn's disease intestinal lamina propria mononuclear cells. *Gastroenterology*. 1997;112(4):1169–1178.
 41. Monteleone G, Monteleone I, Fina D, Vavassori P, Del Vecchio Blanco G, Caruso R, Tersigni R, Alessandrini L, Biancone L, Naccari GC, MacDonald TT, Pallone F. Interleukin-21 enhances T-helper cell type I signaling and interferon-gamma production in Crohn's disease. *Gastroenterology*. 2005;128(3):687–694.
 42. Ordemann J, Jacobi CA, Schwenk W, Stosslein R, Muller JM. Cellular and humoral inflammatory response after laparoscopic and conventional colorectal resections. *Surg Endosc*. 2001;15:600–608.