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Prospective Comparison of Laparoscopic Left Hemicolectomy for Colon Cancer with Laparoscopic Left Hemicolectomy for Benign Colorectal Disease

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Abstract

Background: Short-term outcome and anorectal function results after laparoscopic hemicolectomy for colon cancer were compared with results after laparoscopic hemicolectomy for benign diseases.

Methods: A total of 108 patients who underwent laparoscopic left colectomy (60 for colon cancer, 48 for diverticulitis or polyposis) were enrolled in the study. Left hemicolectomy in patients affected by cancer was performed by high ligation of the inferior mesenteric artery. A questionnaire concerning anorectal function was mailed to patients 6 months after surgery.

Results: Complications were more frequent in the cancer group than in the benign disease group: overall morbidity rate (29.6% versus 8.7%; $P = 0.009$), diarrhea during the first 6 postoperative months (58.7% versus 34.1%; $P = 0.022$), and anorectal function problems (fecal incontinence and/or the inability to discriminate between gas and stool, and/or urgency, and/or tenesmus) (65.2% versus 31.7%; $P = 0.002$).

Discussion: The level of ligation of the lower mesenteric artery and damage at the lower mesenteric ganglion could explain the poorer anorectal function outcome in the colon cancer group.

It is now extensively documented that after an adequate training period, laparoscopic colorectal resection may be performed with reasonable safety standards.[1,2] Most studies carried out to evaluate clinically relevant outcome variables, such as postoperative morbidity and functional anorectal results after laparoscopic colectomy, compare laparoscopic versus open surgery.[3–10] Some clinical trials concern patients affected by colorectal cancer; others concern patients affected with benign diseases, and still others concern case histories including both groups of patients. No study has compared short outcome and postoperative anorectal function results of patients suffering from colorectal cancer and those affected with

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benign diseases who have undergone the same surgical laparoscopic technique. In this prospective study, short-term outcome and anorectal function results after laparoscopic hemicolectomy performed for colon cancer are compared with results after laparoscopic hemicolectomy carried out for benign diseases.

METHODS

From February 2001 to July 2004, adult patients admitted to our department for colorectal disease were assessed for study eligibility. Their physical status was assessed according to the American Society of Anesthesiologists (ASA) score. Patients who had previously undergone major abdominal surgery were not considered suitable for laparoscopic colonic resection. Patients who had undergone appendicectomy, cholecystectomy, hysterectomy, or annexectomy were enrolled in the study, and the previous operation was reported in the database. Inclusion criteria were age at least 18 years and suitability for elective surgery. Exclusion criteria were very high risk for general anaesthesia (ASA IV), pregnancy, cancer infiltrating adjacent organs assessed by computed tomography or magnetic resonance imaging, coagulation disorders, hepatic dysfunction (Child-Pugh class C), ongoing infection, and plasma neutrophil level less than 2.0×10^9/l.

Because one of the aims of the study was the evaluation of postoperative anorectal function, patients with a history of anorectal function problems prior to surgery were excluded from the study. The potential participants had the study design explained and were then required to sign a written informed consent.

On hospital admission, demographics, nutritional status, and primary diagnosis were recorded for all eligible patients. Obesity was defined as body mass index (weight in kilograms/height in meters^2) more than 30.

In all patients, bowel preparation was carried out the day before surgery by intestinal washout with 4 l of polyethylene glycol electrolyte solution. The evening before surgery, patients were given an enema. Systemic prophylactic antibiotics consisting of 750 mg cefuroxime and 500 mg metronidazole were given intravenously at induction of anesthesia. A second dose of the same antibiotics was administered intraoperatively if surgery lasted more than 4 hours. Deep vein thrombosis prophylaxis was carried out with low-molecular-weight heparin (50 IU/kg per day) in all patients. Urinary catheter and nasogastric tubes were routinely used. All patients underwent general anesthesia. General anesthesia was induced with fentanyl (3.5 μg/kg), propofol (2.5 mg/kg), and atracurium (0.5 mg/kg). Anesthesia was maintained with air and oxygen (FiO_2 0.5%), sevoflurane (1.2/2.2%), atracurium (0.5 mg/kg per hour), and fentanyl (0.5/1.5 μg/kg per hour). To maintain normothermia, active intraoperative warming (forced air warming at 38°C on the thorax and upper limbs plus on-line heating) was instituted.

The surgeons (L. S. and L. R.) were experts both in laparoscopic techniques and in open colorectal surgery.

Laparoscopic-assisted left hemicolectomy was a five-trocar standard technique[11] with systematic mobilization of the splenic flexure and resection of the rectosigmoid junction. Pneumoperitoneum was induced by insufflation of CO_2 and was maintained at 12 mmHg during the entire surgical procedure. The extent of demolition was the same, independent of the pathology occasioning surgery; resection was always extended from the distal transverse colon to the upper third of the rectum. The mesenteric vein was ligated at the inferior border of the pancreas; the upper left colonic artery was always transacted to allow sufficient mobilization of the left transverse colon, and the greater omentum was partially detached from the transverse colon. The only difference between the two techniques was in the height of the ligation of the inferior mesenteric artery: left hemicolectomy in patients affected by cancer was performed by high ligation of the inferior mesenteric artery; in patients affected by diverticulitis or polyposis the inferior mesenteric artery was cut just below the branch of the left colonic artery. In all patients, the pelvic autonomic nerve was preserved. The identification and division of the lymphovascular pedicle and the mobilization of colonic segments were carried out by bipolar forceps and monopolar scissors. Mesentery division, distal bowel resection, and a Knight-Griffen mechanical anastomosis between the distal transverse colon and the upper third of the rectum, just under the level of the sacral promontory, were performed intracorporeally; bowel resection was extracorporeal through an enlarged suprapubic trocar site. The specimen was always retrieved in an impermeable bag to prevent tumor spillage or wound contamination. Conversion to open surgery was defined as the need to perform an abdominal incision longer than 7 cm. Patients who had conversion to open surgery were excluded from subsequent evaluations in the study.

The following details of the surgical procedure were recorded in all patients: duration of surgery, operative blood loss, amount of homologous blood transfused. The volume of operative blood loss was calculated by adding the blood aspirated to the weight of the gauzes used during surgery. Transfusion of blood products in the

Table 1.
Demographic and clinical characteristics of patients and type (benign or malignant) of disease occasioning left hemicolectomy

Variable	Colon cancer (n = 60)	Benign diseases (diverticulitis, polyposis) (n = 48)	P Value
Age (years)	68 ± 11.8	56.6 ± 12.0	0.001
Men/women	36/24	21/27	n.s.
ASA score	2.3 ± 0.7	2.1 ± 0.8	n.s.
Haemoglobin (g/L)	12.7 ± 2.3	12.1 ± 2.4	n.s.
Obesity	4 (6.7%)	4 (8.3%)	n.s.

perioperative period was based on the hemoglobin level (< 80 g/l) or on an individual basis according to the clinical condition.

All patients were treated in accordance with a strictly controlled protocol regarding analgesic administration, feeding, and postoperative care. Postoperative analgesia was ensured by continuous intravenous infusion of morphine hydrochlorate (1/2 mg/h) and ketoprophene (300 mg/24 h) . Postoperative recovery of bowel function was evaluated by first flatus and bowel movement. No patient was allowed to resume oral feeding before the first flatus occurred. Trained members of the surgical staff who were not involved in the study registered postoperative complications. They also decided the first day of solid food resumption and the day of hospital discharge.

Microbiologic analysis and positive culture were used to diagnose infectious complications. Any anastomotic dehiscence with clinical and/or radiological evidence was considered. Patients were discharged after meeting the following conditions: bowel movement and full recovery of both ambulation and oral food intake. Follow-up for infectious and non-infectious complications was carried out for 30 days after hospital discharge by weekly surgery visit. Recovery of physical activity was evaluated during surgery visits by asking the patients about working ability, long-distance walking ability, climbing stairs, and lifting heavy objects.

Only patients who underwent surgery at under 75 years of age and after 1990 for stage III colon cancer received adjuvant chemotherapy.[12] The drug regimen for chemotherapy was 375 mg/m^2 per day 5-FU and 20 mg/m^2 per day levamisole, 5 days/week every 4 weeks for 6 months.

A questionnaire concerning anorectal function was mailed to patients 6 months after surgery. Patients with anastomotic leaks were excluded from this part of the study, to avoid possible confusing effects. Patients who had previous cerebrovascular accidents were excluded for the same reasons. The questions concerning anorectal function included the following categories of bowel symptoms: diarrhea; anal incontinence score[13]; inability to discriminate between gas, urgency, tenesmus. The anal incontinence score as described by Pescatori *et al.*,[13] even though not yet validated, gives an indication of the type of incontinence, *i.e.*, incontinent for flatus, liquid, or solid stools; and frequency, ranging from never to every day. Patient replies and clinical data were collected in a computerised database. For the purposes of this study, patients undergoing surgery for diverticulitis and for polyposis were considered together in the group defined as " benign diseases."

Descriptive data are reported as mean ± standard deviation, 95% confidence interval (CI), median and range, or number of patients and percentage. Comparison between groups for discrete variables was made by the chi-squared test or the Fisher exact test when appropriate. The student t-test and analysis of variance for repeated measurements were used to compare normally distributed variables. $P < 0.05$ was considered to indicate statistical significance (two-tailed test). Factors such as disease occasioning surgery and age and sex of patients were included in a stepwise logistic regression multivariate analysis, with the aim of evaluating the possible influence of the latter two factors on the relationship between patient disease and anorectal function problems.

RESULTS

One hundred and thirty five patients were assessed for eligibility for the study; exclusion criteria left 111 patients who were eligible, three of them refusing to participate. Of the 108 patients enrolled in the study, 60 (55.6%) underwent laparoscopic left hemicolectomy for colon cancer, 48 (44.4%) underwent the same operation for benign disease: 45 for diverticulitis and 3 for polyposis. The two groups were well balanced as to ASA score, preoperative haemoglobin and rate of obesity (Table 1), but significantly differed as to age and gender, those undergoing surgery for benign diseases tending to be younger, and more frequently of the female sex (Table 1).

Table 2.
Number of patients with postoperative complications according to type (benign or malignant) of disease occasioning laparoscopic left hemicolectomy without conversion to open surgery

Complications	Colon cancer ($n = 54$[a])	Benign diseases (diverticulitis, polyposis) ($n = 46$[a])	*P* Value
Overall	16 (29.6%)	4 (8.7%)	0.009
Infectious[b]	11 (20.4%)	4 (8.7%)	n.s.
Non-infectious[b]	4 (7.1%)	1 (2.2%)	n.s.
Anastomotic leak[b]	2 (3.7%)	1 (2.2%)	n.s.

[a]In six patients in the colon cancer group and two patients in the benign disease group, conversion to open surgery was necessary. These patients were not considered for data analysis in this table.

[b]Numbers of single type of complication do not add up to the number of overall complications with the two groups, in relation to the possible occurrence of more than one type of complications in some patients.

In six patients (10%) in the cancer group and in two patients (4.2%) in the benign disease group, conversion to open surgery was necessary; however, the difference was not statistically significant. In the cancer group, hemorrhage (2 cases), small bowel injury (2 cases), development of hypercapnia (1 case), or adhesions (1 case) were the reasons for conversion. In the benign disease group, hemorrhage (1 patient) and hypercapnia (1 case) required conversion. These patients were not considered for further data analysis, leaving 100 patients in the study (54 colon cancer cases and 46 benign disease cases). A primary diverting stoma was not fashioned in some patients in the study. The mean operative time was 227.96 ± 40.95 minutes in the cancer group and 233.26 ± 40.06 minutes in the benign group ($P = 0.516$). The mean operative blood loss was 230 ± 107 ml in the cancer group and 203 ± 77 ml in the benign disease group ($P = 0.370$). Nine cancer patients (17.3%) and six patients affected by benign disease (12.5%) received homologous blood transfusion ($P = 0.45$). No patient died in the postoperative course.

Table 2 shows that the overall morbidity rate was higher in the cancer group (29.6%, 95% CI: 23.4–35.8%) than in the benign disease group (8.7%, 95% CI: 0.6–16.8%) ($P = 0.009$). Fewer patients had infectious complications in the benign disease group (8.7%) than in the cancer group (20.4%), although the difference did not result in being significant ($P = 0.103$). Reoperation was necessary in 2 (3.6%) patients in the cancer group (one anastomotic leak, one bowel herniation) and in 1 (2.2%) patient in the group of patients affected by benign diseases (one anastomotic leak) ($P = 0,88$). Table 3 reports the infectious and non-infectious postoperative complications in detail.

The mean length of hospital stay of patients who did not have conversion to open surgery was 10.19 ± 4.22 days (median: 9; range: 6–31) in the colon cancer group and 9.96 ± 4.15 days (median 9, range 6–31) in the benign disease group ($P = 0.786$).

Recovery of bowel function did not differ between the two groups of patients in the study. The first flatus occurred after 2.27 ± 0.9 days in the cancer group versus 2.25 ± 0.98 days in the benign disease group ($P = 0.997$). The first bowel movement occurred 4.3 ± 1.1 days in the cancer group versus 4.5 ± 1.1 days in the benign disease group ($P = 0.797$).

Of 54 patients affected by colon cancer, 20 (37%) completed adjuvant postoperative chemotherapy; no patient had adjuvant radiotherapy.

A questionnaire concerning anorectal function was mailed 6 months after surgery to 95 patients (3 patients who had anastomotic leak and 2 patients who had previous cerebrovascular accidents were excluded). No patient was still receiving chemotherapy when the questionnaire was mailed. A total of 87 patients replied to the questionnaire.

Forty one patients (47.1%) reported having diarrhea during the first 6 months after left hemicolectomy, more frequently in the group of patients affected by colon cancer (58.7%) than in the group of patients affected by benign diseases (34.1%) ($P = 0.022$). Anorectal function problems, considered as a whole (fecal incontinence and/or the inability to discriminate between gas and stool, and/or urgency, and/or tenesmus), were present in 49.4% of patients, more frequently in patients affected by cancer (65.2%) than in those affected by benign diseases (31.7%) ($P = 0.002$, Odds Ratio = 4308, CI 95% 1.745–10.635). Chemotherapy did not influence this result ($P = 0.519$). The sex of patients did not carry significant difference in these two groups, whereas patient age was significantly different (66.98 ± 9.92 in the group of patients affected by cancer versus 60.39 ± 10.56 in the

Table 3.
Postoperative infectious and non-infectious complications in detail, according to type (benign or malignant) of disease occasioning surgery, in patients who underwent laparoscopic left hemicolectomy without conversion to open surgery

Complications	Colon cancer (n = 54)	Benign diseases (diverticulitis, polyposis) (n = 46)
Infectious complications	11 (20.4%)	4 (8.7%)
Wound	5 (9.2%)	2 (4.3%)
Respiratory tract	3 (5.5%)	1 (2.2%)
Urinary tract	2 (3.7%)	1 (2.2%)
Abdominal abscess	1 (1.8%)	0
Non-infectious complications	4 (7.1%)	1 (2.2%)
Delayed gastric emptying	2 (3.7%)	0
Intestinal obstruction	1 (1.8%)	0
Delayed recovery of bowel function	0	1 (2.2%)
Arrhythmia	1 (1.8%)	0

Differences between patients affected by colon cancer and patients affected by benign diseases were not statistically significant.

Table 4.
Anorectal function problems (transient anal incontinence, inability to discriminate between gas and stool, tenesmus, and urgency after left hemicolectomy, according to type (benign or malignant) of disease occasioning surgery

Anorectal function problems	Colon cancer (n = 46)	Benign diseases (diverticulitis, polyposis) (n = 41)	p Value
Transient anal incontinence	17 (37%)	7 (17%)	0.038
Inability to discriminate between gas and stool	15 (32.6%)	9 (21.9%)	0.267
Tenesmus	12 (26.1%)	8 (19.5%)	0.467
Urgency	12 (26.1%)	6 (14.6%)	0.188

group of patients affected by benign disease, $P = 0.004$). For this reason, the results concerning the correlation between disease and anorectal function problems were corrected for age, and the Odds Ratio was 4.176 (CI 95% = 3.728–4.678), demonstrating that age does not influence the result. When data regarding disease occasioning surgery, chemotherapy, and age and sex of patients were included in a stepwise logistic regression multivariate analysis, only patient disease was associated with anorectal function problems ($P < 0.001$, Odds Ratio = 7.438, CI 95% 2.413–22.921).

No patient was affected by anal incontinence 6 months after laparoscopic left hemicolectomy, although 27.6% of patients reported transient early anal incontinence (during the first postoperative months), ranging in severity from 3 to 5 (median 4). Inability to discriminate between gas and stool, tenesmus, and urgency during the first 6 postoperative months was present in 27.6%, 23%, and 20.7% of cases respectively. As Table 4 shows, these anorectal function problems were more frequent in the group of colon cancer patients, although the difference is not statistically significant. Independent of the pathology that had occasioned surgery, the frequency of anorectal function problems resulted in being significantly associated with the presence of postoperative diarrhea ($P = 0.001$).

DISCUSSION

The feasibility and safety of laparoscopic colorectal resection have been repeatedly reported. Laparoscopic surgery seems to be associated with less tissue injury than open surgery. Thus, some benefits can be expected, such as reduced postoperative pain, faster recovery of intestinal motility and function, and shorter hospitalization. This might translate into an improved outcome. Nonetheless, it is difficult to draw any firm conclusions regarding the advantage of laparoscopic colorectal resection based on clinically relevant variables, because the results of published trials are often conflicting.[3–10] There may be several reasons for thid, an important one undoubtedly being the differences in criteria for patient selection. Many large-scale trials, for instance, include both patients undergoing surgery for colorectal cancer

and those operated on for benign diseases. We have hypothesized that the postoperative outcome of patients undergoing the same operation for differing pathologies could differ, and for this reason we have conducted this study in which we compare short-term outcome and anorectal function results after laparoscopic hemicolectomy for colon cancer with the results after the same procedure performed for benign diseases.

The surgical technique employed was the same. The extent of resection that we practice is always the same, independent of the pathology occasioning surgery. In the case of benign diseases, we prefer to proceed to left hemicolectomy, as we do in the case of colon cancer. It has been demonstrated that a shorter length of resected colon specimen is associated with the persistence of preoperative abdominal symptoms in patients affected by diverticulitis,[14] and it has been affirmed that the rectum should be used for anastomosis to avoid recurrence after the surgical treatment of diverticulitis.[15] We cut the inferior mesenteric artery in the case of benign disease without dividing the colon and rectal mesentery, because the removal of the entire mesocolon is simpler, guarantees better hemostasis, and does not cause damage to the autonomous nerves. The only difference between the two techniques is in the height of the ligation of the inferior mesenteric artery: in patients affected by cancer, a high ligation of the inferior mesenteric artery is performed; in those affected by diverticulitis or polyposis, the lower mesenteric artery is cut just below the branch of the left colonic artery.

In the present study, the overall conversion rate was 7.4%, similar to that of other large series[4,16,17] and with no difference between the two groups of patients.

Analysis of the operative variables showed that duration of surgery, operative blood loss, and perioperative homologous transfusion rate were not significantly different in the two groups. It would thus seem that the type of pathology does not have any influence on the difficulty of application of the technique employed. A significant difference was found, on the other hand, by analyzing complication rates. In the present study, the colon cancer group had a significantly higher postoperative complication rate than did the benign disease group. This difference could be attributed to the greater age of patients affected by colon cancer and hence to a higher frequency of comorbidity factors; however, no differences were found in the two groups in the distribution of the ASA score. The most frequent complications reported by patients operated on for colon cancer compared to those undergoing surgery for benign diseases were, above all, of an infective nature. A possible explanation could be a better preservation of systemic immune function in the group of patients with benign diseases. Patients operated on for diverticulitis—most of those undergoing surgery for benign disease—were all operated on at least 2 months from the last episode of acute diverticulitis, when presumably systemic immune function was normal. Patients operated on for colon cancer, on the other hand, were affected by the pathology at the time of surgery and had a greater probability of an altered systemic immune function.

The rate of anastomotic leak and reoperation was not significantly different between the two groups; furthermore, the number of cases is too small for this result to be of statistical significance. Recovery of bowel function and length of hospital stay had a similar pattern.

Patients operated on for cancer had a worse anorectal function outcome. Although no patient was affected by anal incontinence 6 months after laparoscopic left hemicolectomy, 65% of colon cancer patients who underwent surgery had anorectal function problems during the first postoperative 6 months. This observation is not easy to explain; nor is it any easier to interpret the reason for the lower frequency of anorectal function problems after surgery for benign diseases. In both groups of patients, the pelvic autonomic nerve was preserved, and a mechanical anastomosis between the distal transverse colon and the upper third of the rectum, just under the level of the sacral promontory, was used. The level of ligation of the lower mesenteric artery, however, could provide an explanation. When we carry out laparoscopic isolation of the lower mesenteric artery at its origin, we follow the anterior plane of the aortic wall without completely freeing the aorta. In any case, we cauterize with bipolar forceps the structures surrounding the origin of the arterial mesenteric trunk. It could be this laparoscopic maneuver, which is different from that practiced in patients with benign diseases, where the inferior mesenteric artery is cut more distally just below the branch of the left colonic artery, that causes the damage at the lower mesenteric ganglion[18] and the origin of the thoracolumbar sympathetic nerves.[19] This damage, associated with the preservation of the parasympathetic pelvic autonomic nerve, could be responsible for the increased motility of the residual colon and of the rectum, and for the altered functioning of the internal sphincter. Several studies suggest that the human internal anal sphincter receives sympathetic excitatory innervation from the thoracolumbar sympathetic nerves.[20,21] The hypothesis of sympathetic ganglion damage during laparoscopic high ligature of the lower mesenteric artery would seem to be borne out by the observation that, after laparoscopic left

hemicolectomy for cancer, many patients (59%) had diarrhea during the first 6 postoperative months, and that we observed anorectal function problems more often in patients with postoperative diarrhea than in patients with normal stool. In dogs, the resection of ganglion and plexus around the lower mesenteric artery causes contractile abnormalities at the middle and distal colon, with frequent bowel movements and diarrhea.[22]

In conclusion, postoperative outcome of laparoscopic left colectomy differs between patients who underwent surgery for colon cancer and those who underwent colectomy for benign diseases. We thus consider that, independently of the cause of this difference, future studies carried out in order to analyze the results of laparoscopic colorectal surgery should take this fact into account.

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