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Laparoscopic versus open colorectal resections in patients with symptomatic stage IV colorectal cancer

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(1)

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Abstract

Background

The purpose of this study was to evaluate short-term and oncologic outcomes of laparoscopic resection (LR) for patients with symptomatic stage IV colorectal cancer compared with open resection (OR).

Methods

This study is a retrospective analysis of a prospective database. Patients with a minimum follow-up of 12 months after LR or OR for metastatic colorectal cancer were included. All analyses were performed on an “intention-to-treat” basis.

Results

A total of 162 consecutive patients submitted to LR and 127 submitted to OR were included. In the LR group, conversion rate was 26.5 %, mostly due to locally advanced disease (88.4 %). A greater risk of conversion was observed among patients with a tumor size greater than 5 cm regardless the tumor site ($P = 0.07$). Early postoperative outcome was significantly better for LR group, with a shorter hospital stay ($P = 0.008$), earlier onset of adjuvant treatment, and similar postoperative complications ($P = 0.853$) and mortality rates ($P = 0.958$). LR for rectal cancer was associated with a higher morbidity compared with colon cancer ($P = 0.058$). During a median follow-up time of 72 months, there was no significant difference in overall survival between the two groups ($P = 0.622$).

Conclusions

LR for symptomatic metastatic CRC is safe and, compared with OR, is associated with a shorter hospital stay and with similar survival rates. Concerns remain about LR of bulky tumors and rectal cancers due to the increased risk of conversion and postoperative complications.

Keywords

Symptomatic Metastatic Colorectal cancer Laparoscopy

Despite the screening programs that are designed to detect early colorectal cancer (CRC), 15–20 % of patients with colorectal malignancies present distant metastasis at the time of diagnosis [1–4], which are resectable in only approximately 20 % of cases [5].

With the recent advances in chemotherapy, the treatment of asymptomatic metastatic patients is changing. Whereas in case of symptoms, such as bleeding or colonic obstruction, resection of primary tumor is mandatory, the surgical treatment of asymptomatic patients is controversial. Some authors suggest resection of the tumor to prevent complications related to the tumor and to reduce the rate of emergency surgery [6–11]; others prefer to postpone surgery in case of response to neoadjuvant chemotherapy [12, 13].

Few studies have been published concerning the surgical treatment of symptomatic metastatic CRC [14–18], and most of them consisted of only a small number of patients [14–17]. Recent reviews and meta-analysis of the literature [19–22] have confirmed better short-term outcomes of laparoscopic surgery in patients affected by nonmetastatic CRC compared with open surgery. Furthermore, several large, randomized, clinical trials [23–27] have reported equivalent 5 year survival results and recurrence rate between laparoscopic and open surgery for stage I–III colon

cancer. However, data on laparoscopic resection for symptomatic stage IV CRC are still lacking. The purpose of this study was to evaluate short-term and oncologic outcomes of laparoscopic resection for patients with stage IV CRC compared with open surgery.

Materials and methods

This study is a retrospective analysis of a prospective database created in April 1992. All consecutive patients submitted to laparoscopic (LR) or open resection (OR) for symptomatic metastatic CRC at our department during the study period were included in the database. Patients who presented with indications for emergency surgery, such as acute intestinal obstruction or perforation and acute bleeding, were excluded from the study. Absolute contraindications to general anesthesia also were considered exclusion criteria.

Three surgeons performed all the procedures. Two of them (M.M., M.D.) who had extensive experience in advanced laparoscopic techniques used a laparoscopic approach (LR), whereas the third surgeon (G.G.) performed conventional open resection (OR). Therefore, patients underwent laparoscopic or open surgery depending on the referring surgeon. All procedures were performed following the same oncologic guidelines in both groups: adequate resection margins, “en bloc” vascular resection and lymphadenectomy and minimal intraoperative manipulation of the tumor. In the LR group, during right hemicolectomy the specimen was extracted through a small abdominal incision with the use of a wound protector, and an extracorporeal handsewn or stapled anastomosis was performed. During left hemicolectomy, sigmoidectomy, and anterior resection, the specimen was removed through a small suprapubic transverse incision, and the anastomosis was performed by laparoscopic transanal intracorporeal stapled technique.

Preoperative workup was standardized for both groups and included physical examination, total colonoscopy, abdominal CT scan, chest X-ray, and tumor marker blood test for CEA and CA-19.9. For rectal cancer, a pelvic RMI also was required. All patients underwent a preoperative oncologic evaluation to assess the indication for a neoadjuvant treatment.

Pre- and postoperative management was standardized for both groups. Potent oral laxatives, such as polyethylene glycol solution, were used preoperatively until 2005. Intravenous antibiotics, such as second-generation cephalosporins and methronidazole, were administered before incision and continued for 5 days after the operation. Deep venous thrombosis prophylaxis was achieved by administering low-molecular-weight heparins. Postoperative analgesia was ensured by intravenous local anesthetics (bupivacaine) for 48 h and by parenteral nonsteroidal analgesics. Oral intake was started on the day after the first flatus occurred.

Patients were divided in two groups: metastatic laparoscopic (ML) and metastatic open (MO). The following parameters were entered into the database: patient’s characteristics (age, gender, American Society of Anesthesiology (ASA) status, tumor site, and location of metastases), operative variables, pathological data, short-term outcomes, and survival rate. Operative variables included operative time (from skin incision to application of dressings), intraoperative morbidity, and conversion rate. Conversion to laparotomy in case of LR was defined as an unplanned incision or an incision performed longer or earlier than that planned. Pathological data included tumor size, number of lymph nodes harvested, and surgical (circumferential and distal) resection margins. Short-term outcomes included resumption of gastrointestinal functions, length of hospital stay, and morbidity and mortality rates (patient mortality within 30 days after surgery).

Adjuvant chemotherapy was offered to patients on the basis of a clinical oncological evaluation within 8 weeks after surgery; indications, protocols, and regimens of administered adjuvant chemotherapy did not differ between the two groups. All patients were followed up prospectively with clinical examination and serum CEA blood test every 3 months and liver ultrasound every 6 months for the first 2 years, and annually thereafter. Chest X-ray and abdominal CT scan were performed every year. A colonoscopy was performed at 12 months from surgery and every 3 years

thereafter. Data were collected prospectively from the time of diagnosis using a custom-written computerized data base.

Statistical analysis

Quantitative data are given as median and range. Chi-square tests were used to compare proportions. Student's t test was used to compare normally distributed variables. Univariate analyses of overall survival rate were performed using the Kaplan–Meier, method and the evaluation of differences between the groups was performed with the log-rank test. Patients' observations were censored on the date of last examination or death. All analyses were performed on an "intention-to-treat" basis. Patients for whom the LR was converted into OR were analyzed in the LR group. A level of 5 % was set as the criterion for statistical significance. The data were collected in an Excel spreadsheet. The statistical analysis was performed using SYSTAT Version 10[®] (SPSS Inc., 2000).

Results

Between April 1992 and April 2010, 2,074 patients with CRC were admitted to our Institution. Of these, 107 patients were submitted to transanal endoscopic microsurgery and 95 to emergency surgery because of obstruction or bleeding. As a result, 1,872 consecutive patients underwent elective colorectal resection: 1,107 by laparoscopy (LR) and 765 by open approach (OR). Patients presented with metastatic (TNM stage IV) CRC in 162 (14.6 %) LR cases (ML group) and in 127 (16.6 %) OR cases (MO group).

Both groups were well matched for age, sex distribution, ASA status, main presenting symptoms, tumor site, and location of metastases (Table 1). In six patients of the ML group and three patients of the MO group, a peritoneal carcinomatosis was intraoperatively diagnosed. No patient underwent neoadjuvant chemoradiotherapy.

Table 1
Baseline characteristics

| | ML (n = 162) | MO (n = 127) | P value |
|---------------------------|---------------------|---------------------|----------------|
| Gender | | | |
| Male, n (%) | 103 (63.5 %) | 76 (59.8 %) | 0.603 |
| Age (year) | | | |
| Median (range) | 67 (28–88) | 70 (34–88) | 0.186 |
| ASA status, n (%) | | | |
| I | 58 (35.8 %) | 47 (37 %) | 0.93 |
| II | 76 (46.9 %) | 56 (44.1 %) | 0.722 |
| III | 25 (15.4 %) | 20 (15.8 %) | 0.944 |
| IV | 3 (1.9 %) | 4 (3.1 %) | 0.785 |
| Tumor localization, n (%) | | | |
| Cecum | 14 (8.6 %) | 9 (7.1 %) | 0.803 |
| Ascending colon | 24 (14.8 %) | 15 (11.8 %) | 0.57 |
| Transverse colon | 1 (0.6 %) | 3 (2.4 %) | 0.429 |
| Splenic flexure | 5 (3.1 %) | 6 (4.7 %) | 0.835 |

| | ML (n = 162) | MO (n = 127) | P value |
|---------------------------|---------------------|---------------------|----------------|
| Descending colon | 11 (6.8 %) | 7 (5.5 %) | 0.945 |
| Sigmoid colon | 62 (38.3 %) | 50 (39.4 %) | 0.911 |
| Rectum | 45 (27.8 %) | 37 (29.1 %) | 0.429 |
| Site of metastasis, n (%) | | | |
| Liver | 112 (69.1 %) | 84 (66.1 %) | 0.678 |
| Lung | 10 (6.2 %) | 9 (7.1 %) | 0.946 |
| Peritoneum | 9 (5.6 %) | 7 (5.5 %) | 0.824 |
| Bone | 1 (0.6 %) | 1 (0.8 %) | 0.608 |
| Ovary | 2 (1.2 %) | 3 (2.4 %) | 0.747 |
| Multiple | 28 (17.3 %) | 23 (18.1 %) | 0.983 |
| Main presenting symptoms | | | |
| Anemia | 35 (21.6 %) | 24 (18.9 %) | 0.676 |
| Rectal bleeding | 56 (34.6 %) | 51 (40.2 %) | 0.392 |
| Abdominal pain | 33 (20.4 %) | 21 (16.5 %) | 0.489 |
| Constipation | 38 (23.4 %) | 31 (24.4 %) | 0.953 |

ML metastatic laparoscopic group; MO metastatic open group

Peroperative results

A comparable number of left and right hemicolectomies, transverse colon resections, sigmoidectomies, anterior resections, abdominoperineal resections, Hartmann's procedures, segmental resections, and total colectomies were performed in the two groups (Table 2). In all cases, the primary CR malignancy was radically removed. Operative time and blood loss were similar between the two groups. Intraoperative complications rate was 2.4 % in ML group and 1.6 % in MO group ($P = 0.908$). There were 43 (26.5 %) conversions to laparotomy in the ML group because of locally advanced neoplasm in 38 cases (88.4 %), technical difficulties in four cases, and urethral lesion in one case (Table 2). An increased risk of conversion to laparotomy was observed among patients with a tumor size larger than 5 cm (30.9 % vs. 17.6 %, $P = 0.07$), regardless of the tumor site.

Table 2
Operative results

| | Overall (n = 289) | ML (n = 162) | MO (n = 127) | P value * |
|----------------------------|------------------------------|-------------------------|-------------------------|----------------------|
| Procedure, n (%) | | | | |
| Right hemicolectomy | 62 (21.4 %) | 38 (23.5 %) | 24 (18.9 %) | 0.423 |
| Transverse colon resection | 4 (1.4 %) | 1 (0.6 %) | 3 (2.4 %) | 0.429 |
| Left hemicolectomy | 21 (7.3 %) | 12 (7.4 %) | 9 (7.1 %) | 0.896 |
| Sigmoidectomy | 87 (30.1 %) | 52 (32.1 %) | 35 (27.6 %) | 0.485 |
| Anterior resection | 63 (21.8 %) | 36 (22.2 %) | 27 (21.2 %) | 0.951 |
| Abdominoperineal resection | 19 (6.6 %) | 9 (5.6 %) | 10 (7.9 %) | 0.587 |
| Hartmann's procedure | 17 (5.8 %) | 8 (4.9 %) | 9 (7.1 %) | 0.591 |

| | Overall (n = 289) | ML (n = 162) | MO (n = 127) | P value* |
|--|------------------------------|-------------------------|-------------------------|---------------------|
| Segmental resection | 8 (2.8 %) | 4 (2.5 %) | 4 (3.1 %) | 0.958 |
| Total colectomy | 8 (2.8 %) | 2 (1.2 %) | 6 (4.7 %) | 0.148 |
| Operative time (min), median (range) | 125 (75–360) | 130 (75–360) | 120 (70–200) | 0.141 |
| Intraoperative blood loss (ml), median (range) | 110 (30–850) | 100 (30–700) | 110 (50–850) | 0.155 |
| Intraoperative complications, n (%) | 6 (2 %) | 4 (2.4 %) | 2 (1.6 %) | 0.908 |
| Ileocolic twist after right hemicolectomy | 1 (0.3 %) | 1 (0.6 %) | 0 | 0.881 |
| Mesenteric bleeding | 1 (0.3 %) | 1 (0.6 %) | 0 | 0.881 |
| Ureterals lesion | 1 (0.3 %) | 1 (0.6 %) | 0 | 0.881 |
| Atrial fibrillation | 1 (0.3 %) | 1 (0.6 %) | 0 | 0.881 |
| Splenic injury | 2 (0.7 %) | 0 | 2 (1.6%) | 0.365 |
| Conversion to open surgery, n (%) | | 43 (26.5%) | – | |

ML metastatic laparoscopic group; MO metastatic open group

*ML vs. MO

A protective diverting stoma was performed in 17 (47.2 %) anterior resections in the ML group and in 10 (37 %) anterior resections in the MO group (P = 0.581). A synchronous liver resection was performed in nine cases (5.5 %) in the ML group and four cases (3.1 %) in the MO group. No intraoperative morbidity occurred in this group of patients.

Postoperative results

Patients in the ML group showed a significantly earlier time to first flatus (3 vs. 4 days; P < 0.001) and stools (4 vs. 5 days; P < 0.001) than in the MO group (Table 3). There were no statistically significant differences between the two groups in terms of 30 day postoperative morbidity (P = 0.853) and mortality (P = 0.958) rates (Table 3).

Table 3

Postoperative results

| | Overall (n = 289) | ML (n = 162) | MO (n = 127) | P value* |
|-------------------------|------------------------------|-------------------------|-------------------------|---------------------|
| 30-day morbidity, n (%) | 61 (21.1 %) | 33 (20.4 %) | 28 (22 %) | 0.853 |
| Bleeding | 8 (2.8 %) | 2 (1.2 %) | 6 (4.7 %) | 0.148 |
| Wound infection | 8 (2.8 %) | 3 (1.9 %) | 5 (3.9 %) | 0.505 |
| Anastomotic leakage | 15 (5.2 %) | 11 (7.6 %) | 4 (3.7 %) | 0.303 |
| Prolonged ileus | 11 (3.8 %) | 7 (4.3 %) | 4 (3.1 %) | 0.826 |
| Cardiovascular | 3 (1 %) | 0 | 3 (2.4 %) | 0.161 |
| Pulmonary | 8 (2.8 %) | 5 (3.1 %) | 3 (2.4 %) | 0.999 |
| Liver failure | 5 (1.7 %) | 4 (2.5 %) | 1 (0.8 %) | 0.521 |
| Ureterals injury | 1 (0.3 %) | 1 (0.6 %) | 0 | 0.881 |
| Deep vein thrombosis | 2 (0.7 %) | 0 | 2 (1.6 %) | 0.365 |
| Reoperation, n (%) | 11 (3.8 %) | 8 (4.9 %) | 3 (2.4 %) | 0.428 |

| | Overall (n = 289) | ML (n = 162) | MO (n = 127) | P value* |
|--|------------------------------|-------------------------|-------------------------|---------------------|
| 30 day mortality, n (%) | 8 (2.7 %) | 4 (2.4 %) | 4 (3.2 %) | 0.958 |
| Liver failure | 3 (1 %) | 2 (1.2 %) | 1 (0.8 %) | 0.8 |
| Intestinal infarction | 1 (0.35 %) | 1 (0.6 %) | 0 | 0.881 |
| Acute respiratory distress syndrome | 1 (0.35 %) | 1 (0.6 %) | 0 | 0.881 |
| Acute myocardial infarction | 2 (0.7 %) | 0 | 2 (1.6 %) | 0.365 |
| Stroke | 1 (0.3 %) | 0 | 1 (0.8 %) | 0.889 |
| Time to patient's mobilization (day) median, range | 3 (1–6) | 2 (1–5) | 3 (2–6) | <0.001 |
| Time to first flatus (day), median (range) | 3 (1–8) | 3 (1–5) | 4 (2–8) | <0.001 |
| Time to first bowel movement (day), median (range) | 4 (2–10) | 4 (2–9) | 5 (2–10) | <0.001 |
| Hospital stay (day), median (range) | 10 (4–47) | 8 (4–46) | 11 (6–47) | 0.008 |
| Long-term morbidity, n (%) | 3 (1 %) | 2 (1.2 %) | 1 (0.8 %) | 0.8 |
| Anastomotic strictures | 3 | 2 | 1 | |

ML metastatic laparoscopic group; MO metastatic open group

*ML vs. MO

Overall, postoperative morbidity rate was 21.1 % (61/289). In the ML group, there was a higher morbidity rate after surgery for rectal cancer compared with surgery for colon cancer (31.1 %, 14/45 vs. 16.2 %, 19/117; $P = 0.058$). In particular, the anastomotic leakage rate was significantly higher after “sphincter saving” anterior resection compared with colon resection with primary anastomosis (19.4 % vs. 3.6 %, $P = 0.021$). In the MO group, resection for rectal cancer was not associated with a higher morbidity compared with resection for colon cancer (13.5 %, 5/37 vs. 25.6 %, 23/90; $P = 0.21$).

A total of eight patients (four patients in each group) underwent reoperation: an anastomotic leakage treated with a diverting stoma in seven cases (four patients from ML group and three patients from MO group), and one prolonged postoperative ileus treated with intestinal débridement in one patient of the MO group.

The 30 day mortality rate was 2.7 % (8/289) in the whole series; it was 2.4 % (4/162) in the ML group and 3.2 % (4/127) in the MO group. The median hospital stay was significantly shorter in the ML group (eight (range, 4–46) days) than in the MO group (11 (range, 6–47) days; $P = 0.008$).

Multiple sites of metastasis represented a relative risk for postoperative complications in the ML group (28.6 % vs 18.7 %; $P = 0.354$) but not in the MO group (26.1 % vs. 21.2 %; $P = 0.816$).

Among patients with multiple sites of metastasis in the ML group, we recorded four general (two cases of hepatic failure, one case of pulmonary embolism, and one case of pneumonia) and four surgical complications (three anastomotic leakages and one urinary fistula). A reoperation was necessary in two cases for anastomotic leakage. In MO patients with multiple sites of metastasis, three cardiopulmonary complications and three wound infections occurred. Mortality rate was not influenced by multiple sites of metastasis in the ML group (3.6 % vs. 1.8 %, $P = 0.919$) or the MO group (4.3 % vs. 2.9 %, $P = 0.755$).

Pathological results

There were no statistically significant differences between ML and MO group in terms of median tumor size (4 vs. 5 cm, $P = 0.229$) and median number of lymph nodes harvested (13 vs. 13; $P = 0.625$). No positive circumferential or distal resection margins were detected in both groups.

Long-term results

Long-term complications (anastomotic stenosis) occurred in two patients (1.2 %) in the ML group and one patient (0.8 %) in the MO group ($P = 0.8$); in all cases, the stenosis was successfully treated by endoscopic balloon dilatation.

The median follow-up period was 75.5 (range, 12–216) months in the ML group and 72 (range, 12–216) months in the MO group. During this period, 15 (9.2 %) patients were lost to follow-up in the ML group and 11 (8.7 %) in the MO group, respectively.

Ninety-six of 143 patients (67.1 %) in the ML group and 65 of 112 (58 %) in the MO group received adjuvant chemotherapy within 8 weeks. Seven patients in the ML group and three patients in the MO group underwent staged liver resection after chemotherapy.

No port-site or wound recurrences were reported during the follow-up period in both groups.

The overall estimated 5 year survival rate was 8.1 % in the whole group of metastatic patients. It was 7.8 % for ML group and 8.2 % for MO group with a mean survival time of 30.1 and 25.4 months, respectively ($P = 0.622$; Fig. 1).

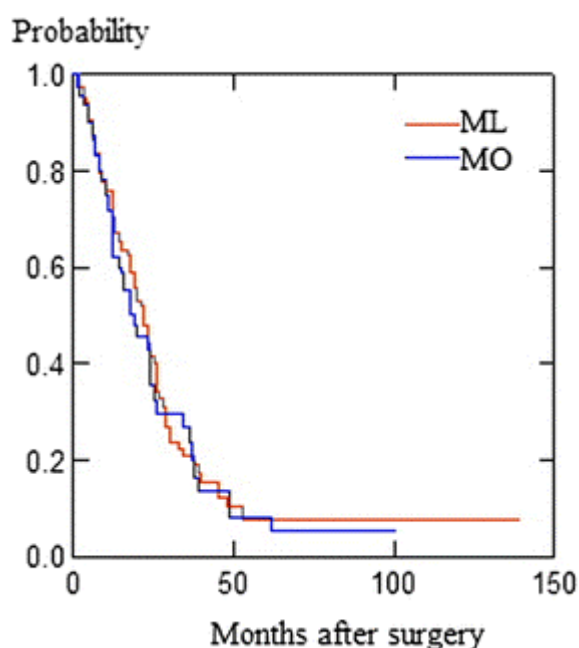


Fig. 1

Overall survival rates for laparoscopic versus open procedures. ML metastatic laparoscopic group; MO metastatic open group. $P = 0.622$, log-rank test

Discussion

The optimal treatment for patients with metastatic CRC is still controversial. The clinical approach to this group of patients depends on several factors, including the site and the extent of metastases, patient's general health conditions, and the presence of symptoms related to the primary tumor (constipation, abdominal pain, bleeding).

A recent meta-analysis was conducted by Stillwell et al. [28] to assess the short- and long-term outcomes of surgical resection in patients with asymptomatic and minimally symptomatic stage IV CRC. The results of this meta-analysis have shown that tumor resection can potentially prolong survival by approximately 6 months, but this survival advantage must be weighed against the likelihood of early postoperative morbidity and mortality. Conventional open surgery for metastatic CRC is associated with a morbidity of 10–42 % [7, 8, 10, 16, 29–34] and a mortality rate of 1.3–10.7 % [8, 9, 30, 32, 34, 35]. The most frequent general complications are cardiopulmonary events (3–7 %), whereas anastomotic leakage represents the most common surgical complication (up to 8 % after colon resection and 24 % after rectal surgery), followed by wound infections. These complications often prolong hospital stay and cause a delay in adjuvant chemotherapy timing. This study shows that overall morbidity and mortality after surgery for symptomatic metastatic CRC are low and similar to those observed after surgery for nonmetastatic disease.

Recent, large, randomized, controlled trials (RCTs) have demonstrated that laparoscopic colon and rectum resection for nonmetastatic cancer does not adversely affect short-term outcomes [36, 37]. However, data on laparoscopic resection for symptomatic stage IV CRC are still limited (Table 4). Two small, retrospective series were published confirming the safety and feasibility of elective LR for symptomatic metastatic CRC.

Table 4

Elective laparoscopic surgery for symptomatic metastatic colorectal cancer: review of the literature

| Author | Patients (n) | Conversions (%) | Morbidity (%) | Mortality (%) | Median survival (mo) |
|--------------------|--------------|-----------------|---------------|---------------|----------------------|
| Milsom et al. [16] | 30 | 10 | 0 | 6.7 | |
| Moloo et al. [17] | 49 | 22 | 14 | 8 | |
| Law et al. [18] | 77 | 13 | 14 | 0 | 16 |
| Current series | 162 | 26.5 | 20.4 | 2.5 | 30.1 |

Milsom et al. [16] reported on 30 patients, 11 of whom had only stoma creation. Three patients were converted to an open procedure. There were no intraoperative complications. Postoperative death occurred in two severely debilitated patients after stoma creation.

Moloo et al. [17] reported their experience of 49 patients with metastatic CRC treated by laparoscopic resection. Conversion rate was 22 %, whereas postoperative mortality rate was 8 % and morbidity rate 14 %. There was no statistically significant difference in terms of mortality and morbidity compared with open surgery for patients with stage I–III cancer.

To the best of our knowledge, only one study has compared laparoscopic to open surgery for symptomatic metastatic colorectal malignancies. Law et al. [18] performed a retrospective analysis of 200 patients with stage IV disease, 77 of whom were submitted to laparoscopic colorectal resection. Conversion was required in ten patients (13 %), and all, except one, conversions were due to fixed or bulky tumors. There was no operative mortality. The complication rate was 14 %, and the median postoperative hospital stay was 7 days. When patients with laparoscopic resection were compared with those with open procedures, the complication rate was significantly lower (14 % vs. 32 %, $P = 0.007$), and the median hospital stay was significantly shorter (7 vs. 8 days, $P = 0.005$) in those submitted to laparoscopic resection. Long-term oncologic results were similar in the two groups.

The current clinical study was designed to compare feasibility, safety, and efficacy of LR versus OR for symptomatic metastatic CRC. Although this is not a prospective, randomized trial, the two groups of patients showed no statistically significant differences in terms of age, ASA status,

symptoms, and tumor and metastasis location. Patients were treated at the same institution and submitted to the same perioperative protocols and therapeutic schedules.

Our results confirm that LR is feasible for the majority of patients submitted to elective resection of metastatic colorectal malignancies. Conversion rate was 26.5 %, which is higher compared with figures reported in randomized, clinical trials on curative LR [36, 37] as well as series on palliative LR [17, 18], ranging from 13 % to 22 %. Because most of these conversions (88.4 %) involved patients with locally advanced disease and tumors ≥ 5 cm in diameter and presented an increased risk of conversion in our experience (30.9 % vs. 17.6 %, $P = 0.07$), it should be discussed whether large, bulky tumors should be approached directly by laparotomy.

In the current study, morbidity and mortality rates in ML group were low and compared favorably with the largest RCT on curative LR [36, 37], confirming the safety of LR also in a palliative setting. Furthermore, there were no significant differences in postoperative morbidity and mortality between LR and OR groups.

Nevertheless, there was a higher morbidity rate after LR for rectal cancer compared with LR for colon cancer (31.1 %, 14/45 vs. 16.2 %, 19/117; $P = 0.058$), with a prolonged postoperative stay in the former group (median, 19 vs. 8 days). These data confirm the suggestion by Kleespies et al. [29], who found rectal site as a highly significant and independent risk factor for postoperative surgical complications in a stage IV setting. They concluded that patients with metastatic rectal cancer are poor candidates for surgery, suggesting local palliation.

Concerning long-term results, only the study published by Law et al. [18] assessed the oncologic efficacy of elective LR for symptomatic metastatic colorectal cancer. They reported a global survival of 16.3 months with no difference between LR and OR. Patients who underwent liver resection had better survival, and the median survival was 30.1 months. In the current study, the overall estimated 5 year survival rate was 7.8 % for ML group and 8.2 % for MO group with a mean survival time of 30.1 and 25.4 months, respectively ($P = 0.622$).

Timing of adjuvant chemotherapy after surgery represents a key factor in survival probability of patients affected by nonmetastatic CRC. Lima et al. [38], reporting 1,053 patients diagnosed with stage III colon adenocarcinoma, demonstrated that those who received adjuvant chemotherapy 12 to 16 weeks after surgery had a 1.43 times higher mortality risk compared with those who received the treatment within 8 weeks and an 18% increase in the risk of colon cancer-specific mortality. Patients who did not receive adjuvant chemotherapy within 16 weeks postsurgery had more than a twofold probability of death compared with those who received it within 8 weeks and had a 76 % increase in the hazard of colon cancer-specific mortality.

In our series, we observed a higher percentage of patients submitted to adjuvant chemotherapy within 8 weeks in ML group, due to a shorter hospital stay and a quicker return to preoperative performance status. The opportunity of an early onset of adjuvant chemotherapy could represent a further theoretical advantage of minimally invasive surgery in metastatic CRC patients compared with open surgery.

Conclusions

This study confirms that elective surgery for symptomatic metastatic CRC is safe; moreover, it suggests that laparoscopic surgery is associated with acceptable morbidity and mortality rates, does not present any oncologic adverse effects, is associated with a shorter hospital stay, and may allow an earlier onset of adjuvant chemotherapy compared with open surgery. Nevertheless, a correct preoperative selection of patients for LR is mandatory to reduce the risk of conversion to laparotomy and therefore to improve the benefits of laparoscopy. The indication to LR should be mainly based on the size and site of the primary tumor; in fact concerns remain about large tumors, because of the higher rate of conversion, and rectal cancers, because of the higher postoperative morbidity rate. These cases should be probably approached directly by laparotomy.

Nevertheless, the lack of randomization and the limited number of patients in the current study do not allow definitive conclusions. Further studies and possibly randomized, controlled trials will be necessary to evaluate the quality-of-life benefits and long-term clinical outcome of LR for patients with metastatic CRC.

Disclosures

Marco Ettore Allaix, Maurizio Degiuli, Giuseppe Giraudo, Alessandra Marano, and Mario Morino have no conflict of interest or financial ties to disclose.

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