Colon cancer: laparoscopic resection

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Introduction

Since the first description by Jacobs [1], laparoscopic colorectal surgery has gained popularity over the past years. The acceptance of this approach has not been as fast as it was for laparoscopic cholecystectomy and other laparoscopic operations, owing to several differences: a steep learning curve of procedures that requires working in multiple abdominal quadrants, control of vascular structures, creation of intestinal anastomoses and sometimes retrieving large specimens [2, 3]. Other concerns have focused on the compliance of oncologic principles of radicality and the presumed increased incidence of port-site metastases described in early series [4]. Several advantages of laparoscopic colorectal surgery have been reported, including reduction of postoperative pain, shortened postoperative ileus and hospital stay, and recently a potential benefit in immune response and oncologic results [5–7].

The objective of this review is to describe the technical issues of laparoscopic-assisted colectomy (LAC) for malignancies, making special reference to the data available on the achievement of oncological principles and the comparison of results with open techniques [8].

Indications

Indications for LAC for colorectal malignancies do not differ from those for open technique. Careful patient evaluation must be done in candidates for LAC. There are important differences in hemodynamic and pulmonary consequences from other laparoscopic procedures. Lloyd-Davis position and prolonged periods of Trendelenburg can particularly affect patients with chronic pulmonary disease [9]. Other patient-related co-morbid conditions must be assessed in the preoperative period. Access problems such as morbid obesity or previous abdominal surgery can offer some difficulties, but do not contraindicate this approach. Several reports have confirmed that previous surgery can extend surgical time, but this has not been related to increased conversion rate [10, 11].

Preoperative tumor evaluation is critical when considering a laparoscopic approach to colorectal cancer. Bulky, large tumors or evidence of adjacent organ infiltration should be carefully analyzed to decide whether laparoscopy is feasible. In our experience, a conversion rate of up to 60% can be expected when there is evidence of adjacent infiltration [10].

The decision to operate on any patient with a malignancy should be based on the surgeon’s expertise in laparoscopic surgery, and conversion should never be viewed as a failure when patients’ safety has to be assured.

Several reports have focused on the steep learning curve of LAC. Some authors have defined absolute numbers to achieve surgical competence as being between 20 and 50 cases [12–15]. However, this definition is biased by the experience of the surgical unit reporting the series. There are critical factors that can affect the learning curve, including the number of cases performed by each surgeon, the time taken to achieve that number and the previous experience in laparoscopic surgery. It has been evident that large series of LAC have come either from high volume colorectal units or high volume endoscopic surgical departments. High volume surgeons do experience less complications and conversion to open approach [3, 10, 15]. A recent study carried out at our unit demonstrated surgical experience, low anterior resection and ASA classification III as independent predictors of conversion. Variables related to malignant disease such as tumor size, preoperative radiotherapy and the need for adjacent organ resection were also significant predictors. As confirmed in other studies, previous abdominal surgery has not influenced conversion in large single-center series.

Technique

Adequate preoperative mechanical bowel preparation and antibiotics are essential. A clear informed consent has to be obtained from each patient that includes information on risk, possible complications and costs. Patients should be advised that long-term benefits of LAC are under study and inclusion in prospective trials is recommended.

Preoperative investigations should include complete blood count, blood chemistry, coagulation status and carcinoembryonic antigen (CEA) level.

With the loss of tactile sensation, special attention should be placed on the tumor location. Small lesions and polyps could present difficulties in a laparoscopic approach so the exact location should be determined with colonoscopy, barium enema or ink tattoo. Several reports have described the need for conversion or resections of normal colon segments owing to the impossibility of locating the lesion [16]. Barium enema can be especially useful to determine the need to descend
the splenic flexure. However, in some cases it is necessary to use intraoperative colonoscopy as laparoscopic assistance and the use of a bowel clamp proximal to the lesion can facilitate the maneuver [17].

An initial laparoscopy should rule out the presence of carcinomatosis and adjacent organ infiltration. Liver assessment can be difficult and laparoscopic ultrasonography is sometimes necessary. In case of right hemicolectomy, the patient is placed in a supine position with the surgeon standing on the left. When performing a sigmoid or rectal resection, the patient is placed in Lloyd-Davis position and the surgeon stands on the right (Figures 1 and 2).

Laparoscopic-assisted colon resections must comply with all the principles of open surgery. Minimum manipulation of the tumor should follow the principles of no-touch technique. Wiggers et al. [18] compared 117 patients undergoing no-touch technique with 119 resections in a conventional way. No-touch technique patients had a significantly lower distant metastases rate in the follow-up.

Another relevant point is the early and proximal ligation of the lympho-vascular pedicle. Left colectomy, sigmoidectomy, low anterior resection or abdominoperineal resections require ligation of inferior mesenteric artery and veins. This can be done with clips or stapling devices after a complete dissection of the perivascular lymph nodes. In the case of a right colectomy the initial approach should identify the duodenum and dissection of the ileocolic artery pedicle.

Tumors located in the transverse colon should be carefully evaluated to determine the operative approach. It is important to decide whether a transverse colectomy is necessary with proximal ligation of the middle colic artery, or an extended right hemicolectomy if the tumor is located towards hepatic flexure, or a left extended hemicolectomy if the tumor is located towards the splenic flexure. An interesting field of research would be to determine sentinel lymph nodes in tumors with no clear vascular dependency.

Incisions for assistance vary between different authors. Location and size should be large enough to prevent the bowel to be forced out, increasing the possibility of injury of the tumor and spreading of malignant cells. Special attention has to be placed on the wound protection and prevention of port-site metastases. Adequate plastic devices can protect the incision for assistance and the absence of leaks from the pneumoperitoneum through the trocars incisions can prevent port-site metastases.

Results of LAC in cancer

Short-term results

Early series in LAC showed no advantage in short-term results of this approach for colorectal malignancies. Bokey et al. [5] reported a series of 61 patients undergoing open or laparoscopic-assisted right hemicolectomy. No difference was observed between groups in outcome, but LAC took longer and was more expensive. Most of these studies were prospective, non-randomized trials from centers with limited experience. More recent studies have reported less need of analgesic use. Hewitt et al. [19] found a significant decrease in morphine requirements between open (62 mg) and LAC (27 mg) in the first 48 h. Early results of the Clinical Outcome of Surgical Therapy study in 449 patients showed LAC requiring less use of both parenteral (mean 3.2 versus 4 days) and oral (mean 1.9 versus 2.2 days) analgesics, and a shorter hospital stay for LAC group (5.6 versus 6.4 days) [20].

Operative time has been consistently longer for LAC in reported series, with most studies showing a mean or median difference of 1 h or more. However, operative time has significantly reduced with the increasing experience [21].

Time to food intake and length of hospital stay have been reported in several studies. A randomized controlled study
showed a mean time of initiation of oral intake of 54 ± 42 h after LAC compared with 85 ± 67 h after open colectomy (P < 0.001) [22]. Recent studies reported a decreased hospital stay. Senagore et al. [23] reported a reduced hospital stay and reduced direct costs in older patients (over 70 years) after LAC compared with traditional open colectomy. A recent meta-analysis that included 12 randomized clinical trials comparing the short-term outcomes of LAC versus open approach in 2512 procedures confirmed lower morbidity and better early results in the laparoscopic approach (less wound infection and need of analgesia, shorter hospital stay). No difference was observed in mortality nor cancer-related variables such as number of lymph nodes and length of the specimen [24].

Oncologic factors. One of the greatest concerns about LAC is the compliance with the oncologic principles of radicality. These requirements include suitable margins, adequate lymph node dissection and the prevention of spillage of cancer cells to either the peritoneal cavity or adjacent lumen of the bowel [26].

Lymph node dissection has been addressed in several reports. None of the studies have found differences in terms of number of lymph nodes recovered. Table 1 show the number of lymph nodes resected in LAC compared with open surgery.

Port-site metastases have been an important issue in the development of LAC. Since Berends’ report in 1994 of the unacceptable rate of 21% of port-site metastases, much research has been carried out in this field identifying factors involved in this kind of recurrence [4]. Technical factors appear to be very important, especially the manipulation of tumor and protection of incision for assistance, instrument contamination, the influence of pneumoperitoneum and aerosolization of malignant cells to the subcutaneous tissue [26].

A dramatic drop in port-site metastases has been reported in recent studies (Table 2), to a rate similar expected as for an open technique (0.7–1.5%) [27, 28], confirming a safe approach. Recently, a large, prospective, randomized trial showed a wound recurrence rate of <1% in patients undergoing LAC [29]. Prevention of port-site recurrence starts with a standard technique avoiding any injury to the colon and minimizing manipulation of the tumor [26, 30]. Pulling large specimens through a small incision should be avoided and the routine protection of the wound with a plastic device can prevent tumor inoculation [31–33].

### Long-term results

Early reports of port-site metastases questioned LAC as a recommended approach. Historical open approach series have reported a 5-year survival of 60% [34]. The most recent data from the National Cancer Institute of the USA report 5-year overall survival rates ranging from 60% to 62% [35]. Medium- to long-term survival results of LAC have been reported recently [36–40]. With a median follow-up of 71 months, 181 patients undergoing LAC for cancer showed a 6% recurrence, with two port-site metastases and a 1% perioperative mortality [41]. Notably, survival rates for the Australian Clinico-Pathological Staging stage C were 74%. Scheidbach et al. [42] published results on 292 patients undergoing laparoscopic-assisted sigmoid resection with a mean follow-up of 2.1 years and a follow-up rate of 73.3%, with a stage-related survival of 88.8%, 90.9% and 64.1% for stages I, II and III respectively. However, it is important to note that laparoscopic-assisted series usually have selected patients, which biases the outcome.

Our unit has published the first randomized trial comparing 106 LAC with 102 open colectomies, with cancer-related survival as the main end point [22]. The mean long-term follow-up was 43 months. Cancer-related mortality was better in the LAC group (9%) compared with the open group (21%) (P <0.02). However, the most interesting result was that LAC seemed to improve the long-term outcome of patients with colon cancer. This difference was due to improvement in survival of stage III tumors.

The large, prospective, multicenter study conducted in 48 institutions in USA included 872 patients randomly assigned to undergo open or laparoscopic-assisted colectomy. At 3 years, the rates of recurrence were similar in the two groups

### Table 1. Lymph node harvest after open and laparoscopic colectomy

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Open (n)</th>
<th>Laparoscopic (%)</th>
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<tbody>
<tr>
<td>Bleday [52]</td>
<td>1993</td>
<td>9.5</td>
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<tr>
<td>Tate [53]</td>
<td>1993</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>Franklin [54]</td>
<td>1996</td>
<td>14.7</td>
<td>15.8</td>
</tr>
<tr>
<td>Lacy [55]</td>
<td>1995</td>
<td>12.5</td>
<td>13</td>
</tr>
<tr>
<td>Goh [56]</td>
<td>1997</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>Milsom [57]</td>
<td>1998</td>
<td>25</td>
<td>19</td>
</tr>
</tbody>
</table>

### Table 2. Port-site metastases and wound recurrence after colon surgery for cancer

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Patients (n)</th>
<th>Incidence (%)</th>
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</thead>
<tbody>
<tr>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hughes [27]</td>
<td>1983</td>
<td>1603</td>
<td>1</td>
</tr>
<tr>
<td>Reilly [28]</td>
<td>1996</td>
<td>1711</td>
<td>0.6</td>
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<tr>
<td>Laparoscopic-assisted colectomy</td>
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<td></td>
<td></td>
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<tr>
<td>Boulez [58]</td>
<td>1996</td>
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<td>2.5</td>
</tr>
<tr>
<td>Hoffman [59]</td>
<td>1996</td>
<td>130</td>
<td>0.8</td>
</tr>
<tr>
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<td>1996</td>
<td>192</td>
<td>0</td>
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<td>2000</td>
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<td>0</td>
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<td>Hartley [49]</td>
<td>2000</td>
<td>57</td>
<td>0</td>
</tr>
<tr>
<td>Lacy [22]</td>
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<td>0.9</td>
</tr>
<tr>
<td>Lumley [41]</td>
<td>2002</td>
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<td>0.6</td>
</tr>
<tr>
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<tr>
<td>Patankar [40]</td>
<td>2003</td>
<td>172</td>
<td>0.6</td>
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</table>
(16% for laparoscopic-assisted and 18% for the open technique) [29]. No long-term data has been published yet from the European multicentre study (COLOR) [43].

**Immune response**

There has been increasing interest in the study of immune response after LAC [44]. Some studies have reported better short-term outcomes of LAC, with different complication rates [7, 23, 45, 46]. Delgado et al. [7] found, in a prospective randomized trial, significant differences in acute phase response between LAC group versus open, expressed as higher levels of interleukin-6 at 4, 12 and 24 h after surgery. In a recent study in 35 patients, Itano et al. [47] found that patients undergoing open colorectal resections had significant suppression of cell-mediated immune response measured by delayed-type hypersensitivity [48]. The clinical significance of this difference could explain lower complication rates and even more, be responsible of a benefit in survival in a selected group of patients undergoing LAC for cancer [22, 49]. Several experimental animal models have demonstrated higher tumor establishment and growth rates after laparotomy than after laparoscopy. Kirman et al. [50] showed in a series of LAC versus open surgery patients a significant decrease in CD31+ T cells in the open group. These T cells are responsible of efficient killing of tumor cells by migrating from the circulation to the peripheral tissues. In a murine model, Carter et al. [51] showed a higher rate of lung metastases after injection of intravenous tumor cells in animals undergoing open coecectomy compared with laparoscopic coectomy. A prospective randomized trial performed in our unit showed better oncologic results in stage III patients undergoing LAC, suggesting that the non-suppressed immune function observed in this group could decrease the chances of tumor metastases [22, 41].

**Summary**

LAC for colon cancer continues to be a topic of debate. However, since its first description more than a decade ago, evidence has clarified topics such as feasibility, safety and recurrence. Port-site metastases have been addressed in recent reports and specific precautions can lower their incidence. It is clear that LAC is associated with shorter hospital stay, less use of analgesia and better cosmesis. A recent large, prospective, randomized trial confirmed that LAC is equivalent to open surgery in terms of oncologic results. There could be an even better result in stage III patients, as described in a recent report [22]. Intense research is underway to study the impact of laparoscopy on cancer biology and immune response that could explain differences in outcome.

**References**


