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Role of minimally invasive surgery in colon cancer: A review

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Abstract

Background: Since laparoscopic surgery was first described for gallbladder disease, a widespread application on other surgical fields has been undeniable. Laparoscopic colectomy (LAC) for benign colorectal disease has slowly gain popularity because of the benefits of this procedure in comparison to the conventional colectomy. Nevertheless LAC for malignant disease is still under investigation. This technique should show the same benefits than open surgery with adherence to the same oncologic principles. Whether this is feasible or not is still an unanswered question.

Objective: To review the current literature of the practice of laparoscopic colectomy in patients with colon carcinoma.

Methods: Selection of the most relevant papers dealing with laparoscopic colectomy for colon cancer was performed on databases such as MEDLINE, PubMed.

Results: The current data shows that LAC in patients with colorectal cancer is a secure procedure with no more risks than conventional surgery in survival and recurrence rates. Although the controversy on the advantages of LAC remains, further studies will be design in the future to address this issue.

Key words: Laparoscopy, colon cancer, colectomy, recurrence, local.

BACKGROUND

Colon cancer is the second most frequent malignancy in the United States and the second most common cause of cancer-related deaths in this country,^{1,2} in Mexico the na-

Resumen

Antecedentes: Desde que la cirugía laparoscópica fue descrita para el tratamiento de patología vesicular, ha sido innegable la gran variedad de aplicaciones de ésta en los diversos campos quirúrgicos. La colectomía laparoscópica (LAC) en enfermedades colorrectales benignas ha ganado lentamente popularidad debido a los beneficios de este procedimiento en comparación con el abordaje convencional. Sin embargo, su uso en cáncer de colon está aún bajo investigación, ya que esta técnica debería mostrar los mismos beneficios que la cirugía abierta en apego a los mismos principios oncológicos. Aún no se sabe si esto es posible o no.

Objetivo: Revisar la literatura actual sobre la práctica de colectomía laparoscópica en pacientes con cáncer de colon.

Métodos: Se realizó una búsqueda en las bases de datos MEDLINE y PubMed seleccionando la literatura más relevante acerca de colectomía laparoscópica por cáncer de colon.

Resultados: La información actual muestra que la LAC en pacientes con cáncer colorrectal es un procedimiento seguro que no confiere mayores riesgos en términos de sobrevida y recurrencia que los de la cirugía convencional. Aunque la controversia sobre las ventajas de la LAC continúa, otros estudios se diseñarán en el futuro para aclarar este punto.

Palabras clave: Laparoscopia, cáncer de colon, recurrencia, local.

tional histopathologic neoplastic registry (RHNN) reported that colon cancer represented 1.8% of all the cancer mortality in the country, and this figure surely underestimates the real number of cases.³

Since the advent of laparoscopic surgery, its influence on the surgical field has been highly important. The most clear example is, without any doubt, cholecystectomy. Since Mouret performed the first laparoscopic cholecystectomy in 1987,⁴ this procedure has emerged as a standard of care and the benefits over open surgery like less hospital stay, and minimum postoperative pain consequence of less surgical trauma are reported in several studies.^{5,6} This has prompted the application of laparoscopic techniques in other procedures like splenectomy and fundoplication.^{7,8} Laparoscopic colectomy (LAC) was first reported by Jacobs et al in 1991⁹ and since, the procedure has been widely used foremost in benign conditions such as inflammatory bowel disease (IBD)

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Abbreviations:

IBD: Inflammatory Bowel Disease

LAC: Laparoscopic colectomy

PSM: Port-site metastasis

SWR: Surgical wound recurrence

and diverticular disease¹⁰⁻¹⁴ because of its aesthetic and functional advantages resuming normal activities quickly¹⁵⁻¹⁹ (*Figure 1*). To perform LAC not only requires formal training with experienced surgeons but advanced laparoscopic skills²⁰ and the steep learning curve can be as high as 70 procedures.^{21,22} One of the reasons that LAC had initially a modest acceptance was because of expensive instrumentation and protracted operating times.²³⁻²⁵ However, once passed the learning curve, the operating time can be reduced up to 50%²⁶ making LAC a feasible, secure, and cost-effective procedure.^{12,27-29} The main debated issue in this area is whether LAC is safe in patients with colon cancer in terms of recurrence rate and long-term survival. When reviewing the data in this area several questions arise: Is LAC the most adequate procedure for patients with curable disease in colon cancer?, Does port-site metastasis (PSM) prohibits the minimally invasive approach?, Is recurrence rate affected by LAC in comparison to the open procedure? Other disadvantages are described like the lack of tactile feedback needed for accurate tumor localization, so an adequate tumor margin can be achieved. The ability of LAC to adhere to several oncologic principles such as adequate lymph node harvesting, length of specimen retrieved, good radial margin are put in doubt because of few large prospective randomized studies. We present a review of the current evidence concerning the application of minimally invasive techniques in patients with colon cancer, outlining certain points of controversy in this issue.

INDICATIONS AND CONTRAINDICATIONS

Even though the indications in benign disease include IBD, diverticular disease, sigmoid volvulus, rectal prolapse and



Figure 1. Postoperative view of a LAR in a patient who had colon cancer. The arrow points out the umbilical scar.

benign polyps the selection criteria in patients with cancer are not well established.^{29,30}

There are studies that support the use of laparoscopic surgery in patients with advanced stage colon cancer for palliative procedures such as stoma formation.^{7,31} But the controversial indication is in those patients in the early stage.⁷

15 to 20% of the patients with colon cancer will present bowel obstruction.^{32,33} In the setting of obstruction, perforation, or any other emergency situation the laparoscopic procedure is not recommended. Also the invasion to adjacent organs and the presence of adhesions that don't allow an adequate colon mobilization is a contraindication.³⁴

The reported mortality of the open procedure in colon cancer for patients above 70 years old is 4%.³⁵ This has prompted the performance of comparative studies between these techniques for older patients, and the results show less mortality in the laparoscopic group³⁶⁻³⁸ and a similar morbidity between patients younger than 60 and older than 80 when submitted to LAC for colorectal cancer. It is the presence of co morbidity more than age itself what leads to higher mortality, thus age is not a contraindication.

PREOPERATIVE MANAGEMENT

The preoperative protocol of LAC does not differ that of the open procedure. It is important to perform mechanical bowel preparation and antibiotic prophylaxis with a cephalosporin like cefuroxime given intravenously at the time of the induction. Localization of the tumor by contrast-imaging studies (i.e. CT, barium enema) and a preoperative colonoscopy is mandatory for delimitation of the segment to be resected.²⁹ Recently a prospective randomized trial compared conventional polyethylene glycol preparation and no preparation, the second group only received one Fleet's enema on the day of the surgery and both preoperative oral antibiotics and perioperative intravenous antibiotics, with no differences in infectious complications between the two groups.^{39,40}

TECHNICAL CONSIDERATIONS

The technique for LAC either the totally laparoscopic (where the restoration of continuity is performed in an intracorporeal fashion) or the laparoscopically assisted (where the anastomosis is performed extracorporeally) has four basic steps: 1) localization of the lesion 2) mobilization of the colon 3) devascularization if the specimen, and 4) specimen retrieval with protection of the wound, and are described in detail elsewhere^{41,42} (*Figure 2*). It is important to adhere to the same oncologic principles of conventional surgery, avoid tumor handling and spillage⁴³ by grasping the bowel by the meso-colon, obtaining adequate resection margin and lymph node

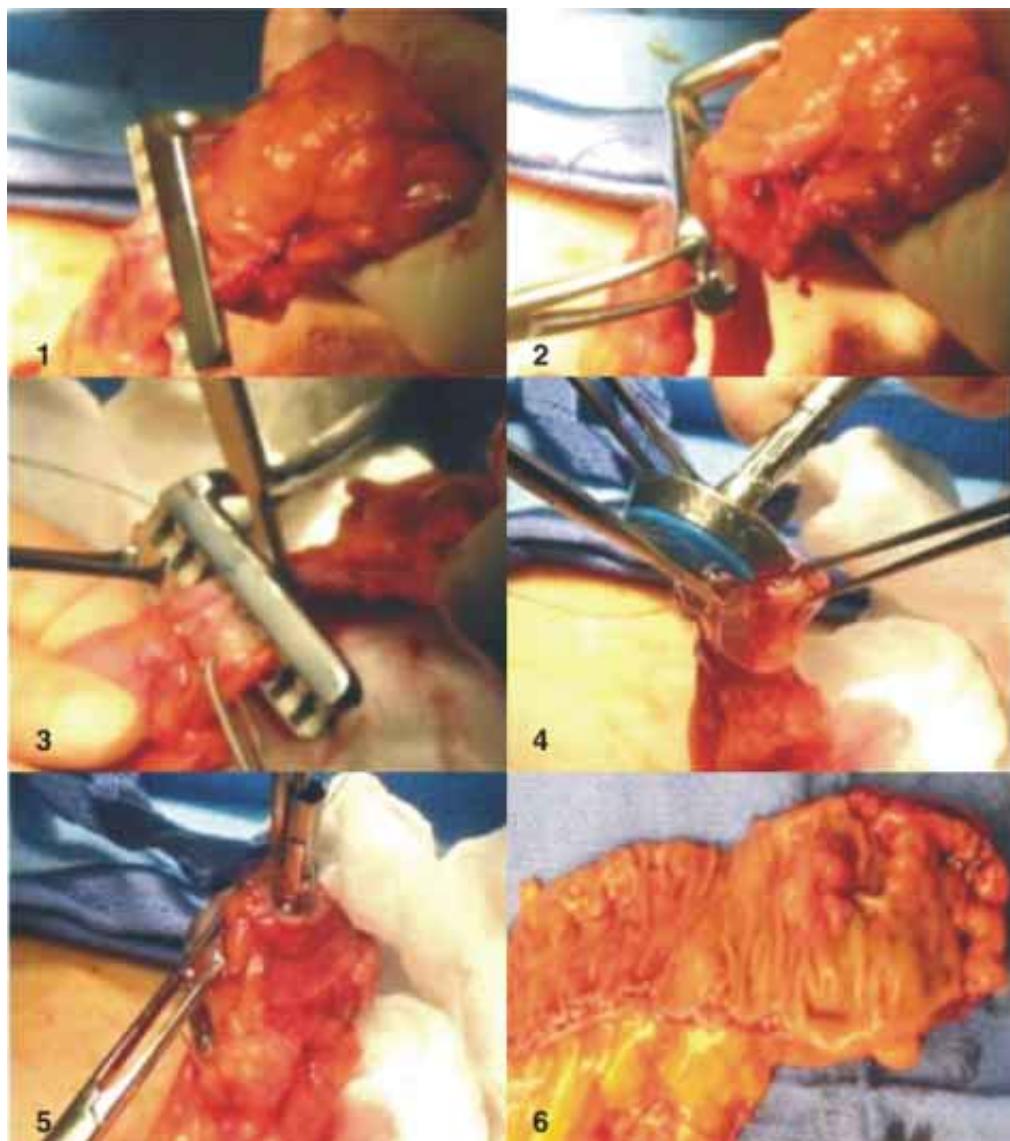


Figure 2. Sequence of events in the extracorporeal time of a laparoscopic colon resection (view text) 1, 2. Use of an automatic purse-string device. 3. Incision of the colon to retrieve the specimen. 4. Insertion of the circular stapler's shaft at the proximal end. 5. Closure of the purse-string suture. 6. Specimen with adequate margins.

harvesting by high division of the colonic vascular supply, perform intraoperative assessment of the stage evaluating liver surface, omentum and bowel and adequate exposure an visualization of iliac vessels and ureter to avoid injury. When the anastomosis is performed extracorporeally the extraction site should be long enough so the retrieval of the specimen is done without any tension to the remaining bowel, and the incision protected by a disposable plastic barrier to avoid seeding of viable tumor cells in the surgical wound^{42,44,45} (*Figures 3 and 4*).

The effect of pneumoperitoneum on bowel microperfusion and oxygenation of the colonic mucosa its not well established.⁴⁶ But studies in animal models show that high-pres-

sure pneumoperitoneum impairs splanchnic perfusion, the clinical impact of this phenomenon is unknown,^{28,47} and the presence of anastomotic leaks relate more with a deficient surgical technique than with the laparoscopic approach.

Preoperative localization of the tumor in LAC is critical and colonoscopy can mark the site of the lesion by way of an endoscopic tattoo, with India ink or indocyanine green, water-soluble dyes are not adequate since they are completely diffused away by 24 h. In some cases the tattoo can not be identified not only because of the localization of the tumor (sometimes the tattoo is oriented towards the retroperitoneum or covered by pericolonic fat) but because of the small amount of ink used and superficial injection.^{48,49} There are

several reports of laparoscopic resection of the wrong segment of the colon.^{50,51} The paper of Vignati et al reports that 86% of the colonoscopies describe accurately the localization of the tumor.⁵² When a transoperative colonoscopy is done the localization can be marked with an endoloop on the serosal surface of the colon.

The conversion rate in LAC for cancer varies from 7 to 28%^{18,53-56} this is because of the experience of the surgeon and some studies do not establish the concept of conversion. A conversion should be acknowledged when the extraction site is lengthened to complete mobilization, devascularization or resection or if a separate incision is required to complete the procedure.

The main predictive factors for conversion are the size of the tumor, patient's weight (> 90 kg), and the surgeon's experience (> 50 LAC's), that's why surgery in patients with body mass index (BMI) above > 35 kg/m² is not recommended.³⁴ In the recent large prospective randomized study



Figure 3. Plastic barrier surrounding the trocar to protect the extraction site.



Figure 4. Right hemicolectomy for colon cancer. A. Note the extraction of the specimen with a segment of the gastrocolic omentum. B. View of the extraction site.

COST the conversion rate was 21% being the most frequent cause advanced disease, since all the surgeons in the study passed rigorous protocol standards, the decrease in conversion rates is therefore a result from a refined process of patient selection rather than from altering oncologic indications from conversions, once the surgeon has passed the learning curve.⁵⁷

RADICALITY IN LAPAROSCOPY

To review the radicality principles in laparoscopy is indeed controversial since oncologic surgery principles bet on an early aggressive treatment when there's a possibility of cure. This situation is not opposite to laparoscopic surgery, that is, to perform a minimally invasive surgery does not mean a minimally resective surgery. The surgeon must acknowledge that the same principles of conventional surgery prevail. It has been demonstrated that the number of lymph nodes harvested in LAC are the same than in the open procedure, moreover there is no difference in the size of the resected specimen.^{26,53,57-60}

The trend of radical resections in oncologic surgery is to include the most amount possible of tumor and surrounding lymphatic tissue, avoiding tumor manipulation. A study by Pezim⁶¹ and Surtees⁶² show that the "high ligation" of the inferior mesenteric artery (therefore a wider resection of lymphatic tissue) does not carry any survival advantage over the ligation at the take-off of the left colic artery. However it is a valid conduct that allows to stage the disease accurately and to determine prognosis.⁶³

In this sense the goals should be the same for both techniques to be able to perform an adequate comparison.

COMPLICATIONS

Laparoscopic complications have been classified by Clavien et al⁶⁴ divided in four grades (*Table 1*). This classification was used in the prospective randomized multicenter COST

Table 1. Classification for laparoscopic complications.

| | |
|---------|--|
| Grade 1 | Non-life threatening and temporary |
| Grade 2 | Potentially life-threatening but temporary |
| Grade 3 | Causing permanent disability |
| Grade 4 | Fatal |

study (Clinical Outcomes of Surgical Therapy Study group)⁵⁷ showing a 20% of complications in the open group and 21% in the laparoscopic group, more than half of the complications were grade 1. Similar results have been reported by other authors.^{7,28,53,65}

The effects of laparoscopic surgery on the immune system are still debatable, it seems that a reduced access-related trauma as seen by a decrease in the immune response is observed in laparoscopic approach, but there's controversial data in this issue.^{54,66}

Other complications such as postoperative ileus, surgical wound infection, pulmonary complications and urinary tract infection are less frequent in LAC patients.^{26,34,67,68} The incidence of anastomotic leaks is similar in both groups.²⁸ In conventional colectomy the incidence of ureteral injury is 0.7% to 5.7%⁶⁹ and 0.2% to 1% in LAC.⁷⁰ Port-site herniation can be avoided by suturing the fascia of the 10 mm port sites.

PORT SITE METASTASIS (PSM)

Since the first report of PSM by Dobronte et al in 1978,⁷¹ the most alarming study, that created great concern was the one of Berends et al⁷² where he reports 3 PSM in 14 patients studied with a PSM rate of 21%. This data provided a compelling rationale for a controlled evaluation, since the PSM rates of LAC for colon cancer in early studies were practically prohibitive.

The first report of PSM in colon cancer was in 1993,⁷³ after which there was growing concern for this phenomenon, putting in doubt the profits of LAC in colon cancer.^{74,75}

There are several postulated theories on the pathogenesis of PSM⁴ (*Table 2*), and are based on the fact that they have occurred in different clinical scenarios, even in early stages of colorectal cancer,^{76,77} or in lateral assistant trocar positions far from the site of tumor extraction, even in cases when no direct tumor handling occurs.⁷⁸⁻⁸⁰

Ziprin et al made a review of 27 studies with at least 50 cases of LAC each and found a 0.71% PSM rate. Currently prospective studies performed by experienced laparoscopic surgeons shows that the rate of recurrence in the surgical wound (SWR) is practically the same as the open procedure.^{4,76,81} The COST study reported a 0.5% in LAC and 0.2% in open surgery.⁵⁷ Although the SWR rate of less of 1% in the conventional procedure^{4,82} is probably underestimated as

Table 2. Potential mechanisms for the development of port-site metastases.

| |
|--|
| Hematogenous spread |
| Direct wound implantation |
| Extraction of specimen |
| Instrument contamination |
| "Chimney effect" |
| Aerosolization of tumor cells |
| Surgical technique |
| Excessive tumor manipulation |
| Surgical experience |
| Effect of the pneumoperitoneum |
| Pressure |
| Effect of CO ₂ |
| Impairment of the host local immune response |

the *post mortem* studies shows a slight increased rate of SWR,⁸³ the most recent review on this issue by Curet concludes that the incidence of PSM in LAC is close to the open procedure but its exact rate remains unknown.⁷⁵ The truth is that the concern has decreased importantly and special attention should be placed in technical aspects of LAC since this is the most important factor for PSM. The measures taken to decrease the PSM rate are controversial and merely experimental (*Table 3*) their effectiveness should be proven in a prospective randomized setting.

RESULTS OF COMPARATIVE CLINICAL STUDIES FOR LAC AND OPEN SURGERY IN COLORECTAL CANCER

The main critic towards LAC in colon cancer is its indication in patients with potentially curable disease, because security in terms of long-term survival rate and recurrence rate has not been proved.⁸⁴ It is estimated that to show a 10% difference in five-year survival, the sample size in each study arm of a trial would need to be 600 (80% power, 5% significance).⁸⁵ Several studies have tried to answer this issue but don't have enough statistical power because of the design (non-randomized, selection bias) or the number of patients.^{26,28,34,53,86,87} Because of this, prospective multicenter randomized trials were design to answer this questions,⁸⁸ like the COST study promoted by the National Cancer Institute in the US.⁵⁷

In the COST study 872 patients with colorectal cancer underwent randomization assigning 437 to the open colectomy group and 435 to the LAC group. This study shows that there is no difference in time to recurrence, overall survival rate and disease-free survival rate between the two groups, and concludes that LAC provides no additional risk of cancer, being an acceptable and safe alternative to open surgery.⁵⁷

Table 3. Suggested techniques for prevention of port site metastases.

| Before resection |
|---|
| Minimize tissue trauma by proper placement of trocars (perpendicularly to peritoneum) |
| Perform trocar fixation |
| Prevent carbon dioxide leakage around trocars |
| Minimize handling of tumor |
| Carry out colonoscopy and intraluminal irrigation with Betadine |
| Clean instruments with Betadine after each use |
| Resection |
| Do not cut through or handle the tumor |
| Perform high-vascular ligature |
| Control colon lumen, especially of resected specimen |
| After resection |
| Irrigate trocars with 5% Betadine before removal |
| Bag the specimen |
| Protect extraction site |
| Drain the peritoneal cavity before deflating, thus preventing the "slosh" phenomenon |
| Perform trocar site closure |
| Deflate the abdomen with the trocars in place |
| Avoid liquid spillage when closing the trocar sites |
| Use closed suction drain |
| Irrigate trocar and extraction sites with Betadine and water |
| Other factors |
| Adequate training |
| Adequate technique |
| Proper patient selection |
| Surgical Team training |
| Adequate laparoscopic equipment for colon resection |

Another prospective randomized study was conducted in Europe, the COLOR trial (Colon carcinoma Laparoscopic or Open resection Trial) was started in 1997 participating 27 hospitals of Sweden, Germany, the Netherlands, France, Italy, Spain and the UK, the data of this study is still to be reported.⁸⁹ Other studies have reported not only advantages in a decreased hospital stay and morbidity but a longer disease-free survival rate.⁹⁰ Initial results small of randomized con-

trolled studies are strengthen by the results of the COST trial.^{16,17,54,55,91-93}

The current data shows that LAC in patients with colorectal cancer is a secure procedure with no more risks than conventional surgery in survival and recurrence rates, nevertheless the controversy on the advantages of LAC remains, since the modest benefits in several reports⁹⁴ (some show no benefits at all),⁹² makes obligatory to design future studies that asses this benefits, because of the controversial data.^{91,93,95}

CONCLUSIONS

Some authors suggest that LAC in colon cancer should not be performed outside a prospective randomized study.^{96,97} Those surgeons with laparoscopic once passed the learning curve to develop enough advanced laparoscopic skills to adhere to the oncologic principles of conventional surgery are the ideal candidates to perform this procedure. If LAC should be offered to colon cancer patients in a general basis is still an training unanswered question. Future studies will give more insight.

We have come a long way since the Swedish surgeon Hans Christian Jacobaeus in 1900 performed a laparoscopy on humans using a rudimentary monocular instrument, the advent of new instruments like the fiberoptic materials, and the high resolution monitors with digitalization of images, allows a wider application of this resource in different medical fields. 13 years ago was impossible to talk about laparoscopic cholecystectomy as an alternative procedure, nowadays is the gold standard for surgical treatment of gallbladder disease.

More changes are to come in minimally invasive surgery and a greater challenge will follow. New applications will stop being experimental to become the standard of care. The german philosopher Arthur Schopenhauer once said: Change alone is eternal, perpetual, immortal. This is certainly the case of laparoscopic surgery in oncologic disease, there will be changes in the future since the ever-evolving nature of medicine carries out new studies.

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