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Role of Minimally Invasive Surgery in Colon Cancer

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Abstract

Colon cancer is a major public health problem. The treatment of colon cancer is primarily surgical using open and minimally invasive techniques. Minimally invasive surgery approaches for colon cancer include single-port laparoscopy, natural orifice transluminal endoscopic surgery, and robotic-assisted laparoscopic surgery. The techniques are based on the same principles: complete mesocolic excision, high vascular ligation, and extended lymphadenectomy. Laparoscopic surgery is characterized by short hospital stay, reduced postoperative pain, and less need for painkillers. Laparoscopic resections are less expensive than open surgery, but with similar quality of life outcomes. Robotic surgery is an alternative to open and laparoscopic techniques. This type of surgery results in a lower conversion rate and a shorter learning curve than laparoscopic surgery. When comparing the clinical outcomes of laparoscopic surgery versus open surgery no difference in disease free survival and overall survival were found. This article shows the role of minimally invasive surgery in colon cancer, the clinical outcomes of laparoscopic and open colon being similar.

Keywords

Colon cancer; Laparoscopic colectomy; Complete mesocolic excision; Minimally Invasive Surgery; Survival

Introduction

Jacobs et al. are the first to report a laparoscopic colectomy in 1991 [1]. The use of laparoscopy in colorectal cancer has been slower paced, though with a lower rate than for cholecystectomy. The initial concerns were related to the safety and efficacy of this technique. Currently, in the United States 40% to 50% of colectomies are performed laparoscopicaly, with a 10% to 20% conversion rate [2].

Laparoscopic colectomy techniques have not been as rapidely adopted as those for laparoscopic cholecystectomy because laparoscopic surgery for colon diseases is associated with a learning curve due to the need to work in all quadrants on a mobile segment, to expose and ligate substantial vascular structures, and the challenge of achieving an intracorporeal anastomosis [3].

Advantages of laparoscopic surgery in colon cancer

Over a period of about two decades, the laparoscopic approach for colorectal cancer resections has evolved from experimental procedures with oncological concern to routine practice. Numerous randomized controlled trials and meta-analyzes have shown that laparoscopic resections are associated with a more rapid recovery, similar oncologic outcomes compared to open surgery both in colon and rectal cancer. Besides improved cosmesis, there are other long-term benefits such as a lower frequency of adhesion-related intestinal obstruction and a lower rate of postoperative hernia [4].

In the USA, only 5% to 10% of 250,000 colectomies are performed laparoscopycally. Laparoscopic colorectal surgery can be successfully performed in patients with benign and malignant diseases, regardless of anatomical location. Laparoscopic resections are associated with a shorter hospital stay, decrease in intravenous narcotic and oral analgesic requirement, with improved quality of life during the first two postoperative weeks. A lower rate of postoperative infections, eventrations, and intestinal obstruction was recorded. The new approach in minimally invasive surgery is single-incision laparoscopic surgery, allowing colorectal resections through a single 2.5 cm incision with excellent cosmetic results [5].

Compared with open surgery, laparoscopic surgery has a number of benefits such as reduced postoperative pain, less postoperative pulmonary and wound complications, decreased blood transfusion requirements, rapid resumption of intestinal transit [6,7], and shorter hospital stay, with similar oncologic outcomes for the two techniques [8]. Laparoscopy provides improved short-term outcomes and at least equivalent long-term outcomes in terms of cancer control when compared with open surgery [9].

Laparoscopic surgery for colorectal cancer is characterized by a learning curve. A systematic review of the literature on the learning curve was conducted using Medline and Embase databases. Of the 23 studies found, 7 studies, representing 4852 cases and 19 surgeons, were analyzed. The factors favoring conversion to open surgery and a higher complication rate were: body mass index, pelvic dissection (for rectal cancer), and male gender. More advanced T stage and the presence of complicated inflammatory disease increase the complexity of cases. This study showed that the length of the learning curve was of 88-152 cases, and case selection criteria can prevent high conversion and complications rate [10].

Patients with various associated comorbidities are not candidates for laparoscopic surgery, as they are considered to be high risk patients. Thus, a group of patients considered high risk, associating one or more such comorbidities as age over 80 years, BMI over 30, heart, lung, kidney, or liver disease and diabetes mellitus, were subjected to laparoscopic colorectal surgery and compared to a group subjected to open surgery. The laparoscopy group had a shorter hospital stay, fewer complications and a lower nonoperative mortality rate. These

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data suggest that laparoscopic colorectal resections can be performed safely in high risk surgical patients, with better outcomes than in those undergoing open surgery [11].

Quality of life is another important aspect in a patient undergoing resection. Quality of life changes and affecting factors were assessed in patients who underwent laparoscopic colectomy for cancer. The affecting factors were tumor stage and chemotherapy, and were more common in male patients. Emotional status improved immediately after surgery, and overall quality of life improved over the first year after laparoscopy, reaching even better levels than before surgery [12].

The cost-effectiveness of each surgery type is analyzed, the more so of minimally invasive techniques. It remains unclear if laparoscopic surgery for colon or rectal cancer is profitable in terms of cost-effectiveness in comparison with open surgery because although laparoscopic surgery results in shorter hospital stay it is associated with higher equipment costs. A thorough analysis of all studies on this topic was conducted. The data were taken from previously published studies and large randomized trials. The cost-effectiveness of laparoscopic surgery versus open surgery for colon and rectal cancer, expressed as cost per quality-adjusted life-year, was measured. The results showed no differences in quality of life between the two surgery types. As to cost-effectiveness, the only thing that advocates the use of laparoscopic resections is the rate of postoperative eventrations. Due to the additional time for incisional hernia repair, laparoscopic resections are more cost-effective if eventration rate remains less than or equal to open resection surgery. The conclusions were that laparoscopic resection for colon cancer is less expensive, with a similar quality of life as with open surgery, and therefore the preferred approach in certain patients [13].

Obesity is a factor that can influence the course of patients undergoing surgery. A study comparing laparoscopic surgical resection for colorectal cancers in obese *versus* non-obese patients showed that in the obese group there was a higher proportion of males, a higher incidence of left colon cancer (49.3 *vs*. 36.8 % , P=0.033) and more associated comorbidities ($P < 0.001$) than in the non-obese group. The length of surgery was significantly longer in the obese *versus* non -obese patients (221 *vs*. 207 min, P=0.025). There were no differences in the overall incidence of postoperative complications between the two groups, however postoperative wound infections were more common in obese patients (P=0.005). Obesity was not a significant independent risk factor for all postoperative complications (P=0.289 [14]. Body mass index was associated with the presence of wound-related complications demonstrating that obesity is a growing risk factor for postoperative complications [15]. Visceral obesity is considered to favor technical difficulty and is a risk factor for postoperative complications in laparoscopic-assisted colectomy. The results showed that a body mass index over 25 and visceral fat area over 100 cm^2 independently predict the incidence of postoperative complications (p=0.040 and 0.007 respectively). Visceral obesity was associated with anastomotic fistula and postoperative infection, and proved a more useful parameter than body mass index in predicting the postoperative course in such patients [16].

Principles of Laparoscopic Surgery

Europe adopted the radical principle of complete mesocolic excision as the optimal therapeutic approach in colon cancer. This concept is similar to total mesorectal excision for rectal cancer and the precise terminology and optimal surgery are key elements. There are three components essential to complete mesocolic excision. The main component involves the dissection between the mesenteric plane and parietal fascia, with the removal of mesentery, mesenteric fascia and visceral peritoneum containing all of the lymph nodes draining the tumor area [17,18].

The second component is a central venous ligation to remove all lymph nodes in vertical direction. The third component is the resection of a suitable length of the bowl to remove the involved pericolic lymph nodes in longitudinal direction. Laparoscopic resection appears to be as adequate to these principles as open surgery [19]. Complete mesocolic excision and high vascular ligation (apical) can improve the course in patients with colon cancer, but none of the analyzed survival parameters was influenced by the type of surgical technique used, classic or laparoscopic [20].

A meta-analysis including all studies from 2009-2011 compared intracorporeal versus extracorporeal anastomosis after laparoscopic right hemicolectomy for cancer. The systematic analysis of the literature included 5 nonrandomized controlled trials including 425 patients which were evaluated for methodological quality. The results showed that intracorporeal anastomosis was associated with a more rapid resumption of intestinal transit, a shorter time to resume eating solid foods, decreased need for pain medication, and a shorter hospital stay. There were no differences in nasogastric tube reintroduction rate, operative time, incision size, total number of nodes harvested, intraoperative complications, mortality, operative complications (anastomotic fistula, anastomotic haemorrhage, wound infection, ileus), reintervention and readmission rate. All these plead for an intracorporeal anastomosis in laparoscopic resections for right-sided colon cancer [21] .

Classification of Laparoscopic Techniques

Colorectal cancer surgery may be performed by open and minimally invasive techniques. Single incision laparoscopic surgery (SILS), natural orifice transluminal endoscopic surgery (NOTES), and robotic-assisted laparoscopic surgery (RALS) are the final points to be reached in minimally invasive surgery [22]. Hand-assisted laparoscopic surgery is a technique that has developed rapidly in the mid-90s after the general introduction of laparoscopy [23]. Although at first this technique was met by reluctance from the laparoscopic community, now it is gaining increasing popularity being considered a bridge towards total laparoscopic colorectal surgery. The technique is easy: a port device is inserted in the abdominal wall which allows surgeon's hand to be introduced into the abdominal cavity while preserving pneumoperitoneum [24].

Single-port laparoscopic surgery is more difficult for sigmoid colon and rectal cancers than for right-sided colon cancers. A study including patients operated by this technique showed that the average duration of surgery was 190 min, average blood loss 20 ml, and no postoperative complications. The average total number lymph nodes harvested was 17, and the distal margin was approximately 58 mm. The procedure was significantly more difficult in the cases in which the sacral promontory protruded ventrally. Depending on tumor location and shape of sacral promontory, the introduction of an additional trocar can render single-port laparoscopic surgery feasible for sigmoid colon and rectal cancer resection [25].

Single-incision laparoscopic surgery is used for right-sided colon cancer. In a study comparing this technique with multiport laparoscopic resections for right hemicolectomy proved that the first technique is a safe approach in this type of colectomy, resulting in a smaller extraction orifice and shorter hospital stay [26]. The safety and efficacy of single-incision laparoscopic resection in stage IV colorectal cancer patients was assessed in a study and the results showed no significant differences in intra- and postoperative complications, 30-day mortality rate, total lymph nodes, and postoperative hospital stay compared to the control group [27].

In addition to single-incision colectomy, to maintain the

minimal invasiveness of this method and the quality of lymph node dissection a new technique, called hybrid single-incision colectomy, has been developed. These techniques resemble, being usual laparoscopic colectomy but excluding a lateral to medial approach. Initial identification or ileocolic vessels exposure was done through a small incision and lymphadenectomy was mainly achieved using laparoscopic techniques. During laparoscopic surgery techniques of open surgery through the small incision may be used. The procedure had no postoperative complications or recurrences and did not require skin incision extension. Operative time was 191 min. This technique is safe and feasible for selected colon cancer patients and is associated with improved cosmesis [28].

Based on recent developments in the field of laparoscopy and endoscopy, a new technique using a combination of laparoscopy and endoscopy was proposed. This technique is named laparoscopic-endoscopic cooperation colorectal surgery and involves removal of a minimal colonic segment being feasible for en block resection of some laterally spreading colonic tumors difficult to resect endoscopically [29].

Natural Orifice Laparoscopy

An abdominal incision is required to extract specimens for laparoscopy-assisted colorectal surgery, incision which brings a number of disadvantages for the surgeon and patient. Natural orifice specimen extraction (NOSE) was developed to avoid these disadvantages. A study analyzing NOSE-type surgery in 24 patients with colon and rectal cancers showed that the average duration of surgery was 110.0 minutes, with an average intraoperative blood loss of 69.1 ml. The time to resumption of intestinal transit for gas was 3.1, days, and mean post-operative hospital stay was 9.2 days. Totally laparoscopic resection with NOSE proved suitable for selected patients with sigmoid colon or rectal cancer, and this technique is worth recommending and wide spreading [30].

Transanal endosopic microsurgery is used in the management of patients with rectal polyps and early-stage rectal cancers [31]. Another minimally invasive technique is laparoscopy-assisted transvaginal resection for sigmoid cancer. With this technique the median number of resected lymph nodes was 15 and the median operative time was 150 minutes; no conversion was necessary and most patients tolerated fluid intake 24 hours after surgery. As to sexual activity in sexually active patients no changes were reported. After a mean follow up of 25 months (10- 41 months) no death or tumor relapse were recorded, suggesting that transvaginal laparoscopy for sigmoid cancer is a feasible and safe technique is in carefully selectewd patients [32].

Laparoscopy-assisted colorectal surgery requires a mini laparotomy for specimen extraction and insertion of the anvil head of circular stapler into the proximal colon. Such mini laparotomy occasionally causes local pain and postoperative infection. To avoid these complications a new technique called complete laparoscopic surgery for colorectal cancer was invented. It uses two techniques: reconstruction by double stapling technique and removal of colon or rectum through the anus. It is restricted to patients with stage T1 cancer after endoscopic resection that allows reconstruction by double stapling and impossible in patients with thin mesentery or anal stenosis. The drawbacks of this technique are bacterial contamination and infection as well as intraluminal spread of exfoliated tumor cells [33].

Robotic Surgery

In recent years, robotic surgery has become a viable alternative to laparoscopic and open surgery in the treatment of colon cancer. The first robotic surgery was performed in 2001 after Food and Drug Administration approved the Da Vinci system in abdominal surgery, and since then its usefulness has increased. Compared with the open techniques, the advantages and superiority of robotic surgery, especially in the pelvis area, have been demonstrated by many studies, being now regarded as a safe and feasible alternative. However, more randomized trials are needed to further assess the favorable oncologic and functional outcomes of robotic surgery [22].

The major advantages of robotic surgery compared with laparoscopic surgery are the lower conversion rate to open surgery and a shorter learning curve. There is evidence to support the fact that in colon cancers laparoscopic surgery and robotic surgery have similar advantages in terms of rapid recovery, although robotic-assisted colectomy is associated with increased costs without providing a clear reduction in the overall morbidity and length of hospital stay [34].

Robotic surgery offers the opportunity to leave behind the limitations of laparoscopic surgery. Three-dimensional visualization and improved dexterity due to flexible instruments should be useful in complex laparoscopic procedures in confined spaces, such as the pelvis. Colorectal resections using the Da Vinci® system are well established and are increasingly becoming standard procedures. The most promising indications are nerve sparing total mesorectal excision in patients with rectal cancer, total mesocolic excision in patients with right-sided colon cancer and rectopexies in patients with pelvic floor insufficiency [35].

Right hemicolectomy with locoregional lymphadenectomy and intracorporeal anastomosis is feasible and can be achieved with this system. Total operative time was approximately 201.4 ± 8.1 minutes, mean robotic time 14.4 ± 7.5 minutes, and the length of hospital stay 8 days. The robotic system has proven to be safe and feasible for carrying out a series of steps: accuracy of nodal dissection, intracorporeal suture of anastomosis, and specimen extraction through natural orifices [36]. In colonic surgery, robotic techniques are associated with increased operative time and higher costs compared with laparoscopic techniques. However, the robot provides a stable camera platform and articulated instruments that eliminate manual tremor. Due to these advantages, robotic systems may play a role in complex procedures such as lymph node dissection around major vessels. In addition, laparoscopy-assisted intracorporeal anastomoses can be easily performed by the surgeon without a substantial need for a competent nurse. Currently, although the short-term and oncologic outcomes of robotic laparoscopic resections are considered acceptable, the long-term outcomes remain unknown [37].

When comparing robotic surgery with laparoscopic surgery in colon cancer resections in terms of short-term outcomes, no significant differences in conversion rate, number of permanent stomies, number of intraoperative complications, level of markers of systemic cellular stress response, number of intraoperative complications, postoperative hospital stay, and postoperative 30-day mortality were found between the two groups. There was a longer preparation time for robotic surgery (77.1 *vs.* 69.7 min, P=0.000), but operative time was significantly shorter with robotic surgery (165.8 *vs.* 183.4 min, P=0.006), without differences in overall procedure time (254.0 *vs.* 243.6 min, P=0.086) [38]. In conclusion, the robotic approach has grown steadily in recent years. The advantage of three-dimensional visualization, improved articulations, and the ability to operate in the pelvis, are theoretical and real advantages in colorectal surgery [39].

Laparoscopy *Versus* Classic Surgery

Between 2000 and 2008 laparoscopic surgeries for colon cancer have increased from 1.5% to 20.7%. As a consequence, the lengths of hospital stay and 28-day readmission rate for colon cancer were reduced. Despite the increase in the number of laparoscopy-assisted resections, the vast majority of colon cancers are treated by open surgery. Laparoscopic surgery reduces the length of hospital stay and

readmission rate, and may result in improved outcomes in terms of colon cancer resection specific survival [40].

Complete mesocolic excision and central vascular ligation for colon cancers can be performed both by open and laparoscopic approach. When comparing the two approaches, the mean time to resumption of normal diet was shorter and the length of hospital stay was significantly shorter (7 days *versus* 13 days, p <0.001) in the laparoscopy groups *versus* open surgery group. The total number of lymph nodes harvested, 30-day operative morbidity, disease-free interval, and 5-year overall survival of the two groups were comparable, without significant statistical differences. The laparoscopic technique proved to be safe and feasible, and in terms short-time outcome it was more advantageous than open surgery [41].

Survival studies have shown that for colon cancer laparoscopic colectomy are safe in terms of short-term outcome, and the long-term oncologic outcomes are not inferior to those from open surgery. Thus, the 5-year recurrence rate, overall survival, and disease-free interval in laparoscopic surgery are similar those from classic surgery [42].

When comparing the long-term outcomes of laparoscopic surgery and classic surgery for TNM stage III colon cancer, laparoscopy was superior with regard to local recurrence or presence of peritoneal carcinomatosis. Open surgery showed a significantly higher probability of local recurrences or metastases (p <0.001), with a significantly increased likelihood of death from neoplastic disease (p=0.001) [43].

The role of laparoscopic surgery for advanced transverse colon cancer remains controversial, especially in terms of long-term oncologic outcomes. When comparing the oncologic outcomes of open surgery and laparoscopy-assisted colectomy the results showed reduced intraoperative blood loss, faster resumption of intestinal transit, and shorter length of postoperative hospital stay in the laparoscopy group. There were no differences in the 5-year survival rate and 5-year disease-free interval between the two groups. Laparoscopy for advanced transverse colon cancer has short-term benefits and equivalent long-term outcomes [44]. Hospital stay after laparoscopic surgery was shorter compared with open surgery (4 days *versus* 7 days). 5-year survival in the laparoscopy group was significantly higher than in the open surgery group (75.8 *versus* 72.5 %, p=0.12), meaning a possible advantage on overall survival [45].

The total number of lymph nodes harvested and of positive lymph nodes was similar in laparoscopy and open surgery patients, with a greater number of total nodes identified in patients with right-sided colon cancer. Other variables such as age, sex, race, or body mass index did not affect the total number of lymph nodes. Lymphadenectomy can be successfully performed by laparoscopic techniques, no demographic factors influencing the outcome [46-48].

All randomized trials of stage I- III colon cancer patients were included in a meta-analysis aimed at comparing the outcomes of laparoscopic and open surgery. In the five trials included in the study no differences in 5-year survival between laparoscopy and open surgery were found, with a trend in favor of open surgery in stage II patients [49]. A meta-analysis evaluated whether the 5-year recurrence and survival rate after laparoscopic colectomy were similar to those after open surgery in colon cancer patients. Five randomized controlled trials involving 2695 patients that reported 5-year survival were included in the meta-analysis. The results showed no significant differences between the two types of surgery in overall mortality (p=0.23), total recurrence rate (p=0.24), 5-year disease-free interval (P=0.96) and 5-year overall survival (P=0.55). This meta-analysis suggests that laparoscopy was as effective and safe as open surgery in colon cancer [50].

Possible Complications in Laparoscopic Surgery

The presence of exfoliated tumor cells in the abdominal cavity is considered to be one of the complications of laparoscopic surgery in colon cancer patients. A study evaluating by cytologic detection the presence of these cells before and after tumor resection showed that laparoscopic surgery does not increase the recurrence and metastasis rate, and survival was similar to open procedure [51].

Chylous ascitis was reported as a possible complication after laparoscopic colorectal cancer surgery. It can occur after right hemicolectomy and left colectomy for sigmoid cancer. Chylous ascitis can occur immediately after resumption of oral food intake, and can be treated conservatively by drainage. If a major lymph duct is involved, it must be ligated or clipped [52].

Another consequence of abdominal surgery is postoperative ileus. A study aimed to assess the duration of postoperative ileus in relation with the type of surgery (open surgery *versus* laparoscopic surgery) showed that in terms of postoperative ileus resolution the open techniques with minimal manipulation of intestinal loops and laparoscopic techniques have similar results [53]. A prospective randomized study investigated the effect of surgery on intestinal permeability, endotoxemia, and bacterial translocation in patients undergoing elective colectomy for colon cancer by comparing classical and laparoscopic surgery. It showed an increase in all monitored parameters, but without statistically significant differences between the two groups [54]. Sigmoid volvulus has also been reported after laparoscopic surgery for sigmoid colon cancer associated with ischemic necrosis of the involved colon segment. The diagnosis was made clinically and by imaging (computed tomography). Treatment consisted in the resection of the necrotic segment and creation of a descending colon stroma. A long remnant sigmoid colon and chronic constipation can contribute to the occurrence of a sigmoid volvulus after laparoscopic resection. Early diagnosis is essential for appropriate treatment and colonoscopy may be useful in detecting ischemic mucosal changes [55].

Most endoscopic surgeries involve carbon dioxide insufflation. It is not uncommon for CO2 to pass spontaneously into the subcutaneous tissue, and later into the bloodstream causing hypercapnia. During laparoscopic surgery, hypercapnia can cause acidosis, arrhythmia, hypotension, myocardial ischemia, and cardiocirculatory arrest [56] and even acute respiratory failure despite endotracheal intubation [57].

Conclusions

The treatment for colon cancer remains surgical. Minimally invasive techniques play an increasingly important role in colorectal cancer resection. The usefulness of laparoscopy has been demonstrated by numerous clinical trials, having similar outcomes compared to open surgery in terms of overall survival and 5-year disease free interval. Laparoscopy is a feasible and safe technique and can be used in the treatment of colon cancer. Robotic surgery is an alternative to laparoscopic surgery, but is associated with much higher costs.

Conflict of Interest

The authors have no conflicts of interest to declare.

Note: The corresponding author is a PhD student at the "Gr. T. Popa" University of Medicine and Pharmacy Iasi. This paper is the result of research during the doctoral internship within the project "Inter-university partnership for increasing the medical doctoral quality and interdisciplinary through doctoral scholarships - DocMed.net" POSDRU/107/1.5/S/78702.

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