Laparoscopic Approach to Colonic Cancer: Critical Appraisal of the Literature

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Key Words

Colonic cancer, laparoscopic approach · Laparoscopic colectomy · Laparoscopic colonic resection · Laparoscopic surgery, review of literature

Abstract

Background/Aims: As laparoscopic colectomy finds its place in the surgical armamentarium, the literature concerning the safety, efficacy, and oncological rationale for treatment of colonic cancer is also enriched. A review and critical appraisal of the literature on this subject was the aim of this paper. **Methods:** A systematic research and a hand search were conducted to gain access to all controlled studies involving laparoscopic colectomy using the Medline, Embase, HealthSTAR, Cumulative Index for Nursing and Allied Health Literature, CancerLit data bases and the Cochrane Central Register of Controlled Trials for the years 1991–2006. **Results:** Over 40 controlled randomized trials and ten systematic reviews and/or meta-analyses were found. Several of the completed controlled randomized trials have published either short- or long-term results; only partial and short-term results are available in rectal cancer. The principal conclusions are that the laparoscopic approach affords better short-term outcomes including surgical site morbidity, but with increased operative times and direct costs. Among the proven long-term outcomes, cancer recurrence and survival do not seem to be worse. Whether conversion, a source of increased operative time and costs, is responsible for poorer

outcomes or whether specific settings associated with poorer outcomes are among the causes of conversion remains to be shown. However, there are still concerns as regards specific laparoscopic-related complications. **Conclusion:** There seems to be no real safety problems in performing laparoscopic colectomy for cancer; improvement in operative times, conversion rates, and complications should make laparoscopy the best cost-effective approach to colectomy.

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Introduction

Colorectal cancer is the fourth most common cancer in both men and women in the USA [1, 2], and the third and second most common cancer for men and women, respectively, in France [3]. Over 130,000 new cases are diagnosed and approximately 50,000 deaths are attributed to colorectal cancer in the USA each year. In France, over 36,000 new cases, representing 15% of all cancers, are diagnosed every year and slightly more than 16,000 patients die each year of colorectal cancer [3].

In the USA, approximately 160,000 colectomies are performed annually, 107,000 (67%) by the open approach, 28,000 (18%) by the hand-assisted approach, and 25,000 (15%) by the purely laparoscopic approach.

In spite of immense progress in the fields of chemotherapy and immunotherapy, surgical resection remains the mainstay of curative treatment for colorectal cancer.

The acceptance of laparoscopic surgery for colonic and rectal cancer, however, has been slow for several reasons: laparoscopic colonic resection (LCR) is technically challenging, involving maneuvers in all four quadrants (retraction of the small bowel and greater omentum, dissection, division of mesenteric blood vessels, and digestive tract anastomosis), new technical skills, the need for extraction of a bulky specimen, along with the use of ever-evolving instrumentation and stapling devices, and finally, fears that LCR could adversely influence outcome. After a shaky start, laparoscopic colorectal surgery is rapidly gaining its credentials, both in benign and now also in malignant disease. The goal of this paper was to cull and review the current literature concerning the laparoscopic approach to colonic cancer, and to critically appraise the available evidence.

Material and Methods

To gain access to all publications, and especially the controlled randomized trials, systematic reviews, and meta-analyses involving laparoscopic (vs. open) colectomy and rectal resections, we performed a systematic research of the electronic literature using the Medline, Embase, HealthSTAR, Cumulative Index for Nursing and Allied Health Literature, CancerLit data bases and the Cochrane Central Register of Controlled Trials for the years 1991–2006. The search strategy was that described by Dickersin and colleagues [4, 5] with the appropriate specific search terms for 'colectomy', 'colonic resection', 'colon', 'intestine-large', 'colonic neoplasm', 'rectum', 'rectal resection', 'proctectomy', 'laparosc*', and 'controlled trials'.

Additionally, the following journals were hand searched: *American Journal of Surgery*, *Archives of Surgery*, *Annals of Surgery*, *British Journal of Surgery*, *Disease of Colon and Rectum*, *International Journal of Colorectal Disease*, *Journal of American College of Surgeons* (formerly *Surgery, Gynecology and Obstetrics*), *Journal of Gastrointestinal Surgery*, *Lancet*, *Langenbeck's Archives of Surgery*, *Surgical Endoscopy*, *Surgical Laparoscopic Endoscopy*, *Surgery*, and the *World Journal of Surgery*.

Results

Over 40 controlled randomized trials were found. Of note, at least eight publications contained duplicated information [6–13] and were not analyzed further. Several other publications were deemed unfit for analysis because of absence of clinical data [14], faulty randomization [15] and three other trials because they involved different anastomotic techniques during laparoscopic sigmoidectomy [16] or compared hand-assisted laparoscopy to laparoscopy [17] and differences between gasless lapa-

roscopy and pneumoperitoneum during laparoscopic colectomy [18].

Ten systematic reviews and/or meta-analyses were found [19–28].

Among the controlled randomized trials underway in the world, several have been published, either as long-term [29–33] or short-term results [34–37]. Several other publications have dealt with partial results, or specific issues of these same or other individual studies [38–46].

As concerns rectal cancer, there are only partial and short-term results available in two trials [34, 39], and we did not analyze the results further.

The major conclusion of these studies is that feasibility of laparoscopic colectomy has been shown to be safe, with advantageous immediate surgical site complications (compared to open colectomy), reasonable morbidity and mortality, as well as long-term carcinological outcomes. The probability of less incisional hernia in the long term, as well as the ease of repair of trocar incisional hernia, compared with the difficult and recurrence-prone repair of incisional hernia after open colectomy may prove to be the major advantage of laparoscopic colectomy. Conversions rate range between 11 and 29% in the randomized controlled trials. Conversion leads to increased operative times and costs. Whether conversion is responsible for poorer outcomes or whether specific settings associated with poorer outcomes are among the causes of conversion remains to be shown. However, there are still concerns as regards increased costs, including longer operative times, and specific laparoscopic-related complications.

Discussion

The safety and technical feasibility of LCR has slowly been confirmed [47–49]. Several non-randomized [50–61] as well as randomized studies [30–36] have underscored that the minimal invasive approach to colectomy decreased postoperative pain with reduction in narcotic usage, and lead to earlier ambulation, faster return to bowel function and oral intake, as well as earlier hospital discharge.

Most of the above-mentioned benefits, however, although reproducible, are modest. Moreover, these classical endpoints were not used in most studies to calculate the power of their trials, and therefore the use of these endpoints to demonstrate the superiority of one technique over the other is highly debatable.

Comparative studies whose design allows patients to have different pain scores just because they are in one or another arm are ethically criticizable: all efforts today should be concentrated on reducing postoperative pain for all patients. The differences could then be the quantity of analgesics necessary so that pain scores would be minimal but equal. When, however, the results of the studies that looked at the difference in the quantity of analgesics necessary are analyzed, the differences were minimal without much clinical relevance: no statistically significant difference in the EORTC pain scores [34], difference of 1 day (median) in duration of parenteral narcotic or oral analgesic use [33], difference of 2.4 injections of morphine (mean) less on day 1 [32], difference of 3–14 of 1,082 patients requiring analgesic use [36]. Patients should be blinded to the approach (never mentioned in any of the controlled randomized trials).

Faster return to bowel function and oral intake has long been highlighted as an advantage of the laparoscopic approach over the open technique. Recent studies seem to indicate, however, that the difference in postoperative recovery may be less significant when perioperative care is optimized [38, 43, 46, 62]. Clearly, fast-track programs have shown that early return of bowel function and oral intake can be achieved even with open colectomy [38, 62, 63]. The same is true for the use of thoracic epidural anesthesia-analgesia [43]. Two recent randomized trials have provided contradictory results. Basse et al. [38], in a study of 60 patients, did not find any significant difference in postoperative recovery parameters. On the other hand, a more recent study by King et al. [42] showed that there was a shorter recovery period and hospital stay when fast-track or enhanced recovery care was instigated in LCR. In a recent systematic review [64], the combined results of six papers (three randomized controlled and three controlled clinical trials), including 512 patients found that both the primary hospital stay and morbidity (relative risk 0.54, 95% CI 0.42–0.69) were significantly lower for such programs. Higher readmission rates, on the other hand, a potential trade-off for shorter hospital stay, were not significantly different (relative risk 1.17, 95% CI 0.73–1.86). Mortality was not found to be increased. Last, the subjectivity that is used to determine hospital discharge is a confounding factor that cannot be ignored any longer. This criterion is of limited value unless the person who decides the hospital discharge (and probably the patient as well) was blinded to the type of approach that was allocated. This has not been reported as such in the case of any of the randomized trials.

Laparoscopy and Cancer

Surgical resection remains the gold standard to cure colon cancer. LCR must be able to achieve the same oncological resection attained by open resection. The problems today are how to reduce the conversion rate, maintaining a high-quality oncological resection, while containing costs.

Conversion

The conversion rate for laparoscopic surgery has been reported to range from 4.2% [65] to 77% [66, 67]. The conversion rate in the controlled randomized trials ranges between 4.2 and 29% [31–34, 36, 39].

Several authors have found that the conversion rate decreased with experience [47, 68]. In a historical control study, Schwandner et al. [69] reported conversion rates of 9.3% for the first 150 procedures and 5.3% for the second 150 operations. In the retrospective multicenter German survey of 1,658 patients, Marusch et al. [68] found that surgeons with experience involving more than 100 laparoscopic colonic operations were more likely to embark on more difficult cases with a conversion rate of 4.3%, as compared with 6.9% for surgeons with experience involving fewer than 100 procedures. Surgeon seniority or experience, represented by the number of operations performed, was established as an independent risk factor for conversion by Tekkis et al. [70]: junior surgeons were shown to be 1.5 times more likely to convert to an open procedure, after adjustment for other confounding variables. On the other hand, according to the data analyzed by Gervaz et al. [66], surgeon experience seems to have little influence on the overall rate of conversion, at least in the studies included in their meta-analysis.

The potentially adverse effects of conversion have been highlighted ever since the report of Slim et al. [71]. These include worse morbidity and mortality [71, 72], worse outcome [34], increased operative time, prolonged hospital stay [72], poorer survival [28, 36, 73], increased need for transfusion [34], and increased costs [40]. While it is certainly possible that these poor outcomes were the consequence of conversion, it might also be that the reasons for conversion could possibly have a part in determining these adverse outcomes, for instance, a large tumor, adhering to the abdominal wall, considered as a poor prognostic factor, could be the cause for conversion. Two groups have looked at independent risk factors for conversion [70, 74]. Both found that increased BMI and surgeon experience were independent risk factors. The other independent risk factors found included malignancy [74] and type of resection (low rectal, left colorectal, right co-

lonic vs. small/other bowel procedures and presence of intraoperative abscess [70]. Of note, abscess and fistula as related to perforation carry a particularly worse influence on prognosis [75].

The recommendations of Belizon et al. [72] warrant reflection: prompt conversion to open (<30 min into operation) significantly reduced postoperative morbidity which leads some to distinguish between early (<30 min) and late (>30 min) conversions [72]. The former are due to difficulties in access, intraoperative discovery of contraindication to LCR (see later), or early complications. The latter are essentially due to (late) intraoperative complications, impossibility to perform the anastomosis or extract the specimen.

Although some of the conversion rates may be considered by some as high, the conversion rates listed in such controlled trials have to be considered as representative of results of the average surgeon performing laparoscopic surgery in our era. Moreover, as underscored by Gervaz et al. [66], when a precise definition is used to define what the authors mean by conversion, the rate is always and statistically significantly higher than when the opposite is true. However, it is difficult to assess the conversion rate as such, and to compare the rate between studies, because of lack of a standard definition. As well, it is difficult if not impossible to take into consideration the variability of surgical skill, experience, and subjectivity which is so important in determining when the surgeon decides to 'convert'.

As concerns the definition, Tekkis et al. [70] proposed talking about conversion when there was a need for a midline laparotomy >10 cm, for either completion of the operative procedure or extraction of the specimen. Casillas et al. [76], once masses >10 cm had been eliminated, defined conversion as any incision >10 cm, or operating through the incision if <10 cm. Others consider conversion to mean any incision exceeding 7 cm [39]. Still others [47, 50] have used a much vaguer definition: 'deviation from the operative plan requiring a major abdominal incision to complete the procedure', or 'an unplanned laparotomy (median laparotomy and Pfannenstiel incision) or an incision made longer or earlier than planned (6 cm is implied) [69].

One paper [49] went to greater details to avoid the use of an incision length in the definition of conversion and to subdue the subjectivity in the decision to 'convert': these authors defined conversion as any operation during which mobilization of the colon and its mesentery or performance of the anastomosis requires additional length of incision (including widening the incision necessary to

extract the specimen), or, without extension of the incision, when 'additional mobilization or unsuspected steps' are necessary to complete the operation.

Oncological Quality of Laparoscopic Resections

By convention, the oncological adequacy of resection for colon cancer is defined by the parameters of *length of bowel resected to yield tumor-free margins* and the *number of lymph nodes* harvested in the specimen. Curative resection is often expressed as a R0 resection (no macroscopically visible tumor left behind) [77]. Several randomized studies [31–33, 44] have shown that laparoscopy can achieve the same curative resection as open surgery. In the meta-analysis by Korolija et al. [23], which looked at 35 studies with data on lymph node count and distal margin clearance (total of 3,935 patients) published between 1990 and 1999, including 16 comparative studies, 6 open series, and 13 laparoscopic series, the average distal margin clearance was 4.6 cm with the laparoscopic approach and 5.3 cm with the open approach. This difference was statistically significant in favor of the open approach. Further, there were more lymph nodes extracted laparoscopically (0.3–2.14 more). This difference was statistically significant only for the fixed-effects single-outcome model; as these studies were heterogeneous in quality, this is somewhat methodologically debatable. Schwenk et al. [26], in their meta-analysis, considered only the results of seven randomly controlled trials (688 participants) and found that there were no significant differences between the two groups either as concerned the length of resected specimen (2 trials, 134 cancer patients) (weighted mean difference (WMD): 0.71 [95% CI –2.05 to 3.48; $p = 0.61$] or the number of lymph nodes: RR = 0.12 [95% CI –1.17 to 1.41; $p = 0.86$]), thus confirming the findings of Korolija et al. [23], but with sounder methodology.

In addition to the resection of the primary cancer, surgical exploration should provide valuable additional information as to the stage of the cancer. Clinically and radiologically unrecognized peritoneal metastases can be as easily identified and biopsied during laparoscopic surgery as in open resection [24]. On the other hand, accurate detection of liver involvement through preoperative imaging studies, such as computed tomography (CT), CT arterial portography, and magnetic resonance imaging with and without injection of contrast material, while improving at a rapid rate, still lack sensitivity for small lesions in the liver [78–80]. Intraoperative laparoscopic ultrasound has been touted to fill the void left by the inability to palpate the liver at laparoscopy [81, 82]. Of note,

however, unsuspected tumor invasion or inadequate pre-operative evaluation was the reason for conversion in 25 of 435 (28% of conversions) [33], 20 of 167 (43% of conversions) [32], 52 of 536 (57% of conversions) [36] and 40 of 246 (66% of conversions) [34] patients in the controlled studies, respectively. This underscores the need for better workup before embarking on laparoscopic resection for all-comers.

Surgical Site or Port-Site Recurrences

The ominous report by Berends et al. [83], who reported a 21% incidence of port-site recurrences and raised the possibility that the pneumoperitoneum somehow altered the pattern of spread and local wound biology, created great concern in the laparoscopic surgical community [84]. Several other studies of different size and design have also dealt with wound recurrence after laparoscopic resections [6, 9, 31, 51, 54, 56, 58, 61, 85–89]. More recent data from large series (single institutions with over 100 patients and multi-institution series with over 400 patients), however, showed that the wound recurrence rate was in reality between 0 and 2.4%, somewhat comparable to what had been reported in open colectomy, ranging from 0.9 to 3.3% [35, 78, 87, 90–92]. At least five prospective randomized trials have shown that the incidence of wound recurrence was not a major issue [27, 31, 33, 36, 44].

Survival

As we are dealing with cancer, survival should be the major endpoint. Three-year survival data are now available for at least four controlled randomized trials [31–34]. In this chapter we will review the data of three of these trials [31–33], criticizing their strong points and weaknesses.

Among the trials presently available for analysis, the Barcelona trial [31] was designed as an ‘equivalency’ trial; the COST trial [33] was a ‘non-inferiority’ trial, whereas the Hong Kong [32], COLOR [36], and the CLASICC [34] studies were designed as ‘superiority’ trials.

Except for the Lacy study, the RCT have shown that laparoscopic colectomy is at least equivalent to open colectomy as concerns oncological surgery. Short-term advantages include fewer surgical site complications, and were touted to require fewer analgesics with better short-term convalescence. However, all laparoscopic procedures took longer to perform.

In fact, all these trials have several important shortcomings that warrant mention. Three RCT [31, 32, 39] were monocenter studies, and as such, results are perhaps

not applicable to other surgical populations, or other surgical teams. The COST, COLOR and CLASICC trials were multicenter studies, and wide applicability is therefore better fitted.

The Lacy study, the only one to show any statistically significant difference in cancer-related survival, was severely criticized for several methodological flaws [93–95], which along with some personal remarks, are summarized hereafter. Let it be said that the response by Lacy [96] was hardly convincing. The main criticisms include: (1) Partial results of the same patient population were published in other publications [9] (91 patients included from November 1993 through January 1996) before the final results were published in *Lancet* in 2002 perhaps influencing the way patients, and assessors, envisioned the follow-up period. (2) Inconsistencies between the previous, partially published results and the final paper in 2002 including: (a) difference in the number of exclusions because of distant metastases (20 [9] vs. 11 [31]); (b) differences in the number or overlap of recruitment periods [7, 97], and (c) differences in the indications for patients receiving chemotherapy: Dukes’ stage B2 and C only [9] vs. routine chemotherapy for stages II and III [31]. (3) Of 442 eligible patients, only 219 were randomized. While the reasons for not including these patients in the study are given, no information as to their outcome was provided. (4) Postoperative chemotherapy was administered to 68 (61%) in the laparoscopic group and to 59 (55%) in the conventional group (difference statistically nonsignificant but lopsided in the same direction as the favorable outcome) and not included in the multivariate analysis, to determine whether it was an independent variable or not. On the other hand, adjuvant chemotherapy was given to 68 of 79 stage II or III patients in the laparoscopy group, but only to 59 of 84 stage II and III patients in the conventional group ($p = 0.023$, two-sided Fisher’s exact test) which might have influenced the outcome. (5) Further oncological concerns include: (a) absence of reported complete (R0) tumor resection rate (especially since there were twice as many patients with T4 tumors in the conventional group), (b) absence of outcome in patients with liver metastases (excluded after randomization) or with locally incomplete tumor resection. (6) Other methodological concerns include: (a) failure to mention the upper and lower limits of the two-sided interval characteristic of the equivalence study, (b) subgroup analysis to state that laparoscopic treatment was better than open, and (c) (if we admit that cancer-free survival is the complement of 100% cancer-related death) the actual difference in cancer-free survival was

$(100-9) = 91\% - (100-21) = 79\% = 12\%$, well under the 15% interval the authors set up to determine that there was a difference, (d) analysis did not adhere to the intention-to-treat principle. (7) Finally, no autopsies seemed to have been performed to ensure that the patients deceased were for reasons unrelated to carcinoma.

The Clinical Outcomes of Surgical Therapy Study Group, or COST study [33], a multicenter, non-inferiority trial, found that there was no statistically significant difference at 3 years in the rates of recurrence (16% for LCR vs. 18% OC; two-sided $p = 0.32$; hazard ratio for recurrence, 0.86; 95% CI 0.63–1.17), the overall survival rate (86 vs. 85%, respectively; $p = 0.51$), or the time to recurrence or overall survival irrespective of the stage of cancer.

Among the criticisms reported [98], we note: (1) absence of definition of the non-inferiority boundary ($-\Delta$ to 0); (2) the statistical methods used correspond to failed superiority trial, and (3) if one considers non-inferiority to be when the upper limit of the one-sided 95% CI for hazard ratio is less than the non-inferiority boundary, the conclusion could be that there was as much as a 16% increase in risk of death and a 11% increase in risk of recurrence in the laparoscopic group. Moreover, it is not clear how many patients had their anastomosis performed laparoscopically.

The monocenter Leung study [32] involved only left-sided cancer. In this superiority trial, the authors found no significant differences in the probabilities of survival at 5 years (76.1% (standard error of the mean: 3.7%) and 72.9% (4.0%), respectively), of being disease-free at 5 years (75.3% (3.7%) and 78.3% (3.7%), respectively). The 95% CI for the difference in 5-year survival was -7.5 to 13.9% , compatible outcome for laparoscopic resection ranging from 7.5% worse survival to 13.9% better survival than open resection. The difference sought was 15%, only just outside the confidence interval. Once again, the number of patients at risk at 5 years was 104 or $104/403 = 26\%$.

Of note, the number of patients available for 5-year follow-up in these three trials was 25.7%. Both of these trials [31, 33], as well as the COLOR and CLASICC studies for which only short-term results are available, included a high proportion of right colectomies (47% for the Lacy trial, 54% for the COST trial, 47% for the COLOR, and 46% for the 313 colonic resections in the CLASICC trial). Right colectomy differs greatly from left colectomy in its performance, oncological tactics, immediate outcome, and difficulties [99–101].

The Braga study [29] did not provide the necessary calculations as to the number of patients necessary. There were no statistically significant differences in overall or disease-free survival.

All in all, while there certainly is a tendency to show that survival is at least not worse with LCR, the methodological flaws in these studies are such that they do not allow to reach these conclusions yet, but only to infer that these outcomes are true. Longer and more complete follow-up results are eagerly awaited for these trials.

Costs, Quality of Life following Hospital Discharge, and Long-Term Surgical-Site Outcomes

Costs

Of the studies available in the literature, most were cost-minimization studies. While some have found that costs were increased by laparoscopic colectomy relative to open colectomy (difference in AUD 1,183 ($p = 0.001$) [102], difference in USD 2,000 ($p = 0.02$) [103]), three of the studies, which looked at direct costs, gave quite different results. One study [104] found an advantage for laparoscopic surgery of USD $3,655 - 3,299 = 356$ ($p = 0.0034$), another [42] found no difference, while a third, the Hong Kong study [32], found that laparoscopic surgery was USD 2,149 more expensive ($p < 0.001$).

Two cost minimization studies looked at subsets of the COLOR ($n = 210$) [41] and CLASICC ($n = 682$) [40]. Both confirmed that operative and overall costs were higher in LRC. Other hospital (non-OR) costs were lower in LCR. Other findings included: higher average cost to individuals for reoperations in LCR, cost of first admission, and total cost to the healthcare system. In another cost minimization study, King et al. [42] compared short-term outcomes of 62 patients, demographically similar, randomized on a 2:1 basis to receive laparoscopic ($n = 43$) or open ($n = 19$) resection of colorectal cancer within an enhanced recovery program. The length of hospital stay ($p = 0.018$), the combined hospital, convalescent, and readmission stay ($p = 0.012$) were shorter for LCR.

Two cost-benefit analyses, one randomized [105] and the other retrospective [106], concluded the LCR took longer to perform, hospital stay was shorter. The randomized study showed that overall morbidity rate was better after LCR 18.2 versus 34.7% ($p < 0.0005$) and that the better postoperative short-term outcome in patients receiving LCR played a key role to nearly balance the operative room charges due to laparoscopy [105]. The sec-

ond [106] showed that total hospital costs were significantly lower for LCR compared with open colectomy and that LCR was cost-effective resulting in significant savings to the healthcare system.

These five papers are important because they underline that LCR should provide great benefits both to the patient and to the healthcare systems, as long as the complication rate stays low, and probably, also, if an enhanced recovery program is used. However, as concerns the shorter hospital stay taken individually, no conclusions can be made, as it is well known that without blinding, hospital discharge should not be used as a surrogate for recovery. This was the main criticism for all the above-mentioned studies.

Quality of Life

In the COST trial [37], one of the earliest to look at this aspect, data for 449 consecutive patients with clinically resectable colon cancer showed better global rating scale scores for 2 weeks postsurgery in LCR vs. OC ($p = 0.009$). While in the hospital, patients assigned to LCR (vs. OC) required fewer days of both parenteral analgesics ($p < 0.001$) and oral analgesics ($p = 0.03$). The short-term quality of life (QOL) benefit was statistically and very moderately clinically significant in LCR at 2 weeks only. Later, these benefits disappeared.

Janson [107] assessed the QOL in patients from the COLOR trial using a cancer-specific questionnaire. The laparoscopic patients fared better on the social functioning component of the EORTC QLQ-30 score at 2 and 4 weeks and on the role function component at 2 weeks.

Braga et al. [29] also looked at QOL as related to long-term complications and survival rate ($n = 391$). Overall QOL was significantly better in the LCR during the first 12 months after surgery, associated with a lower incidence of long-term complications, whereas at 24 months LCR patients reported a significant advantage only in social functioning.

In the CLASICC multicenter clinical trial [34], EORTC QLQ-C30 scores for global QOL and functional scales showed that there was no significant difference at 2 weeks and 3 months.

Possible reasons for this disparity in results include the accrual mode, which was selective in the Weeks study [37], perhaps introducing a selection bias, as well as the fact that in the COST study, the number of inclusions per center was low compared with the COLOR study.

Additional advantages of the laparoscopic route for colectomy include effective palliative resection for pa-

tients with locally advanced, or stage 4 cancer [30, 108], laparoscopic stoma confection in these same patients with locally advanced or recurrent cancer, allowing commencement of chemoradiation treatment as rapidly as possible [109]. The avoidance of a major laparotomy in this setting is clearly desirable.

Most likely, one of the until now little publicized advantages of laparoscopic surgery should logically be less long-term surgical site morbidity, that is less postoperative incisional hernia. Although there is no grade 1 evidence to substantiate this claim, let it be said that most authors admit a 1–19% incisional hernia rate for all surgical site wounds [110, 111], but some have reported as high as a 20% rate for colonic interventions [45], depending on the quality and length of follow-up. The published rates of incision hernia after laparoscopic surgery range between 0.65 and 2.80% overall [112, 113] and between 0.6 [114] and 4.7% [29] for colorectal disease. Of note, one study [45] looked at 83 patients in their institution participating in a large multicenter randomized trial (37 LCR and 46 OCR). Seven patients in the LCR group had been converted to OCR. Surgical site infections occurred in 13.5% of patients after LCR (2.7% trocar, 10.8% extraction sites) and in 10.9% of patients after OCR. During a mean follow-up of 30.1 ± 17.8 months, incisional hernias developed in 24.3% of patients after LCR and in 17.4% after OCR. In the LCR group, extraction sites accounted for 85.7% of all wound complications. The authors concluded that the extraction site for LCR was associated with a high incidence of complications, comparable to open colectomy, and stressed that strategies to alter operative technique should be considered to reduce the incidence of these complications.

Future Endeavors

Long-term results are needed for all of the patients entered into the randomized trials. Efforts have been made to lump together the outcomes of the Lacy, COST, CLASICC, and COLOR trials, as concerns the short-term, and soon, hopefully the long-term survival outcomes. Trials are needed to indicate the best way to decrease the operating time and other direct costs that plague laparoscopic colectomy for the moment. For these reasons, four further controlled randomized studies [115–118] warrant closer analysis.

Marcello et al. [115] compared laparoscopic vascular staplers and disposable clip applicators with the LigaSure Atlas during elective right, left, and total colectomy (152 vessels ligated vs. 169 vessels sealed with the LigaSure).

Table 1. Outcomes according to four controlled randomized studies [115–118]

	Targarona et al. [118]	Morino et al. [116]	Marcello et al. [115]	Takada et al. [117]
Comparison	ES: dissection with ES, vessels clipped vs. CBBE completed by 10-mm LIG vs. 5-mm UC for bowel dissection, vascular pedicle dissection, and meso-colon transaction Mesenteric vessel pedicle controlled with endostapler	UC vs. standard ES	S/C vs. LIG	CBBE vs. US
Number of patients (pts); vessels (v)	38 pts	171 pts	48 pts 152 v vs. 52 pts 169 v	30 pts
Failure/rebleeding			14 (9.2%) of 152 vs. 5 (3%) of 169	0.3 vs. 1.2 (TC); 0.3 vs. 2.0 (Sig)
Blood loss	Less with conventional ES vs. UC or CBBE	UC 140.8 ml vs. ES 182.6 ml (p = 0.032)	50 ml (20–50) vs. 100 ml (25–800) (p = 0.054)	
Costs	NS		USD 317 ± 0 vs. USD 400 ± 112 (p < 0.001)	
Operative time	Longer with conventional ES vs. UC or CBBE	UC 93 min vs. ES 102.6 min (p = 0.46)		7.9 vs. 18.4 min, 15.0 vs. 27.6 min

ES = Electrosurgery; UC = ultracision (harmonic scapel); S/C = vascular staplers and disposable clip appliers; LIG = LigaSure Atlas; CBBE = computed-based bipolar energy; TC = transverse colectomy; Sig = sigmoidectomy.

Morino et al. [116] assessed the safety and efficacy of the ultrasonic dissection (UC) compared with standard electrosurgery (ES) in 171 patients undergoing laparoscopic colorectal surgery. Takada et al. [117] compared the effectiveness of three different energy sources on the laparoscopic performance of a left colectomy in 38 non-selected patients requiring an elective segmental left-sided colon resection: ES plus clips; bipolar ES completed by 10-mm LigaSure; 5-mm ultrasonic shears (Harmonic Scapel). Targarona et al. [118] conducted a comparative study in 30 patients with colon cancer who underwent laparoscopic colectomy using either the electrothermal bipolar vessel sealer (EBVS) or the ultrasonic coagulating shears (UCS).

Outcomes are provided in table 1. Operative time was shorter when the ultrasonic device (US) or EBVS were used vs. electrocoagulation and vessel clips [117], and when EBVS was compared to the UCS (US) [118]. Blood loss was less when US or EBVS were used vs. electrocoagulation and vessel clips [117], when EBVS was used vs. vascular staplers and clips [115] and when US was used vs. standard ES [116], and less rebleeding when EBVS was

compared with vascular staplers and clips [115] or US [118].

In conclusion, energy-driven devices, although they may increase direct costs, are valuable tools to help keep the morbidity to a minimum.

Conclusions

There is now sufficient evidence to show that laparoscopic colectomy is feasible and safe, when performed without excessive complication rates and according to sound oncological principles. The immediate benefits seem to be real, but marginal. Long-term surgical site benefits are probable but remain to be proven. The specter of inordinate surgical site recurrence is no longer a major concern for laparoscopic surgery. The oncological outcome following laparoscopic resections seems at least equivalent to that after open colectomy. All must be done to reduce costs, operative times and conversion rates, and immediate morbidity so that the long-term advantages may surface.

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