

Laparoscopic Procedures for Colon and Rectal Cancer Surgery

Sang W. Lee, M.D.¹

ABSTRACT

After over a decade of debate and controversy, it is now well established that laparoscopic colon surgery for cancer when compared with open surgery, results in short-term benefits while maintaining at least equivalent long-term outcomes. Consequently, more and more patients are undergoing laparoscopic colon surgery, but the adoption rate still remains relatively low in the United States. Similarly, there are many potential benefits to performing rectal surgery laparoscopically. Although not well documented, laparoscopic rectal surgery is under active investigation and may result in the usual short-term benefits associated with laparoscopic surgery. In this article, short- and long-term outcomes of patients undergoing laparoscopic colorectal surgery for cancer are reviewed. In addition, different technical options for laparoscopic approaches to colon and rectal cancer are compared.

KEYWORDS: Colorectal cancer, laparoscopy, hand-assisted colectomy, straight laparoscopy

Objectives: On completion of this article, the reader should be able to discuss laparoscopic procedures for colon and rectal diseases.

Since its introduction, laparoscopic surgery has quickly become the standard of care for many benign indications. Yet the use of laparoscopic techniques for the curative resection of malignancies has been slow to adopt due to initial concerns that it may not be possible to perform an adequate resection laparoscopically and early reports of high rates of port-site tumor recurrences.¹ Based on these initial concerns, a large number of randomized controlled trials have been performed to investigate the long-term outcomes of patients undergoing laparoscopic surgery for colon cancer. After over a decade of debate and controversy, it is now well established that laparoscopic surgery for colon cancer when compared with traditional open surgery, results in short-term benefits such as less pain, shorter length of stay, and

faster return of bowel function while maintaining equivalent oncologic outcomes.²⁻⁵ For this reason, increasing numbers of colon cancer patients are undergoing laparoscopic surgery.

There are many potential benefits of performing rectal surgery laparoscopically as well. Although not well documented, laparoscopic rectal surgery is under active investigation and will likely result in the usual short-term benefits associated with laparoscopic surgery. Oncologic outcomes of rectal cancer patients have been shown to depend on the skills and techniques of the performing surgeons.⁶ A concern is whether technical challenges of laparoscopy may further add to the variability in outcomes. In this chapter, we will review short- and long-term outcomes of patients undergoing

¹Division of Colon and Rectal Surgery, New York Presbyterian Hospital, Weill-Cornell Medical College, New York, New York.

Address for correspondence and reprint requests: Sang W. Lee, M.D., Division of Colon and Rectal Surgery, New York Presbyterian Hospital, Weill-Cornell Medical College, 525 East 68th St., Box 172, New York, NY 10021 (e-mail: sal2013@med.cornell.edu).

Colorectal Cancer; Guest Editor, Robin P. Boushey, M.D., Ph.D.

Clin Colon Rectal Surg 2009;22:218-224. Copyright © 2009 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662.

DOI 10.1055/s-0029-1242461. ISSN 1531-0043.

laparoscopic colorectal surgery for cancer. We will also compare different technical options for laparoscopic approaches to colon and rectal cancer.

SYSTEMIC ONCOLOGIC BENEFITS

Well before human trials data became available, a vast amount of basic science studies have demonstrated that oncologic and immunologic functions are much better preserved after laparoscopic surgery.⁷⁻⁹ These studies suggest that in the right setting, laparoscopic surgery will result in better long-term oncologic outcomes in patients. Why would you expect better oncologic outcomes after laparoscopic surgery? Tumor cells are routinely found both in systemic circulation as well as in the peritoneal fluid immediately following colon cancer surgeries.¹⁰ Whether tumors cells will survive and result in potential recurrence is determined by a tumor's ability to escape body's defenses. Surgical trauma causes significant physiologic alterations in the body's immunologic defenses, rendering patients vulnerable during this critical perioperative period.⁷⁻⁹ By significantly reducing incisional trauma, laparoscopy may result in better preservation of cellular immunity in all phases, decreased stimulation of proliferative growth factors for cancer cells, and decreased angiogenesis.^{7-9,11} Although most of these changes are short-lived, some changes may persist for several months or longer.¹¹ Interestingly, these potential advantages have not been translated into better long-term outcomes in human settings. The only randomized control trial that showed oncologic benefits after laparoscopy was the Barcelona trial. Lacy et al⁴ reported longer cancer-related survival and less tumor recurrences after laparoscopy in patients with stage III disease. All of the other large prospective multicenter trials did not demonstrate long-term oncologic outcomes in favor of laparoscopy.^{2,3,5} Why did we not see improved oncologic outcomes in human settings? Some may argue that all of the controlled trials were done at a time when even the "expert surgeons" who participated in the trials at the time were relatively inexperienced. It has been well documented that a learning curve extends well beyond 20 cases, a prerequisite number of cases required for participating in all of the randomized colon trials.¹² The rates of conversion to open surgery in all three multicenter prospective trials were unexpectedly very high: the NCI Clinical Outcomes of Surgical Therapies (COST; 21%), Colon Cancer Laparoscopic or Open Resection (COLOR; 17%), and the Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (CLASICC; 29%).^{2,3,5} High rates of conversion may reflect a cautious attitude of surgeons performing a new surgical technique with a potentially harmful outcome, but they also may represent relative inexperience of the participating surgeons at the time.

Whether a more up-to-date trial by more experienced laparoscopic colon surgeons will result in better long-term cancer outcomes is debatable. In 2007, Law et al compared outcomes of patients who underwent laparoscopic and open surgeries for cancer. They compared outcomes of 1134 patients who underwent colectomy for colon cancer in two consecutive periods (period 1: 1996–2000; period 2: 2000–2004). During the first period ($N=448$), only open resections were offered to the patients. During the second period ($N=656$), laparoscopic surgeries were offered as an option. The authors found that the 3-year overall survival for patients with nondisseminated diseases decreased significantly during period 2 when compared with those from period 1, while the overall survival who underwent open colectomy remained constant over the two periods.¹³ The authors concluded that there was improvement of survival with the practice of laparoscopic surgery. Although this was not a randomized control trial, its results are intriguing.

PORT WOUND TUMORS

Reports of high incidences of port site tumor recurrences early in the experience of laparoscopic surgery for colon cancer raised serious concerns regarding its safety.¹ The etiology of port wound tumor formations is unclear. Experimental studies suggest that port wound tumors are related to poor surgical techniques and tumor biology. Initially reported incidences were alarmingly high, as high as 21%.¹⁴ Wound tumors also develop after open colectomy for cancer. Hughes et al¹⁵ performed a retrospective review of 1603 colon cancer patients and found the incidence of incisional tumors to be 0.68%.

In 2007, Fleshman et al reported tumor recurrence rates based on the NCI COST trial's 5-year follow-up data. Patients were followed for 8 years with 5-year follow-up data available for 90% of the patients. Wound tumor recurrences were similar for the two groups: 0.5% in the open colectomy group and 0.9% in the laparoscopic group.² Similar outcomes were also observed in the Barcelona trial. In 2008, Lacy et al reported no difference in port tumor recurrence rates between the two study groups based on their long-term data. In this study, median follow-up was 95 months. Only one patient out of 106 laparoscopic patients developed port site metastasis. None of the open patients ($N=102$) developed wound metastases.⁴ In 2009, the European randomized controlled study, the Colon Cancer Laparoscopic or Open Resection (COLOR) trial, reported their rates of tumor recurrences. The median follow-up of this study was 53 months. Port tumor recurrences were found in 7 of 534 (1.3%) patients who had been assigned to laparoscopic colectomy and in 2 of 542 of patients (0.4%) who had been assigned to open colectomy ($p=0.09$). In the laparoscopic group,

five of the seven tumors were at trocar sites whereas two were at the extraction site.⁵

It appears that expected high rates of port tumor recurrences are not observed in the latest updates of all large randomized controlled trials.

Now that we have many studies justifying the use of laparoscopic surgery for colon cancer, increasingly more colon cancer surgeries are being performed laparoscopically. As more surgeons attempt laparoscopic surgeries for cancer, there is a concern for resurgence of high port wound tumor recurrence. More than ever, proper training and observance of safe oncologic techniques are essential. Routine use of wound protectors, limitation of instrument exchanges, avoidance of direct trauma to tumors and inadvertent desufflation events should be practiced.

LAPAROSCOPY FOR COLON CANCER

Purported benefits of laparoscopic surgery include decreased pain, shorter length of stay, quicker return of bowel function, quicker recovery, and decreased wound infection rate. These are justification enough for performing laparoscopic surgery for benign indications but prior to its application for cancer, at least equivalent long-term oncologic outcomes must be demonstrated. Critics of laparoscopic surgery initially questioned whether adequate oncologic resection can be performed laparoscopically. All of the randomized controlled trials demonstrated that there is no difference in surgical margins or number of lymph nodes harvested between laparoscopic and open groups.²⁻⁵ It certainly appears that current laparoscopic methods allow for an equivalent cancer resection when compared with open surgery results.

It was reports of high incidence of port site tumor recurrence early in the experience of laparoscopic surgery for colon cancer that halted its adoption and stimulated organization of randomized trials.¹ As discussed previously, all of the prospective randomized trials demonstrated that expected high rates of port site tumor recurrences are not observed even after 5 years of follow-up.^{2,4} Although these results are important, the most critical outcomes for cancer patients undergoing surgery are survival rates and tumor recurrences.

Short-Term Outcomes

There are at least five major randomized controlled trials that compared laparoscopic versus open surgery for colon cancer: the Milsom trial, Barcelona trial, COST (the U.S.) trial, COLOR (European) trial, and CLASICC (U.K.) trial.^{2-5,16} All of these studies reported similar short-term-outcome advantages associated with laparoscopic surgery. Laparoscopic colon surgery was associ-

ated with a significantly lower intensity of pain, less narcotic use and estimated blood loss, shorter postoperative ileus and length of stay. The Barcelona trial was the only one of these trials to show a significant decrease in postoperative morbidity rate after laparoscopy (11%) compared with open (29%, $p < 0.001$).⁴ Another consistent finding among these studies was significantly longer operative time for the laparoscopic surgery group.

Postoperative recovery of pulmonary function has been shown to be quicker after laparoscopic colectomy in several studies. Milsom et al¹⁶ in a randomized trial showed that pulmonary function as measured by the forced expiratory volume (FEV₁) and forced vital capacity (FVC) improved significantly faster in the laparoscopic than in the open group (3 versus 6 days).

None of the randomized trials showed significant difference in anastomotic leakage rates or wound infection rates between the laparoscopic and open groups.^{2-5,16}

Hand-Assisted Laparoscopic Surgery

One way to potentially decrease operative time while maintaining benefits of laparoscopic surgery may be to use hand-assisted laparoscopic technique. Hand-assisted laparoscopic devices allow placement of a hand into the abdomen while maintaining pneumoperitoneum. This allows preservation of proprioception and tactile feedback and ability to perform manual dissection and retraction. Marcello and the minimally invasive therapeutic trial (MITT) group reported their results from a multicenter prospective trial in 2008. This study was designed to detect a 30-minute reduction in operative time between hand-assisted versus straight laparoscopic sigmoidectomy. The hand-assisted sigmoidectomy group ($N=33$) had significantly shorter operative time (175 ± 58 minutes) when compared with straight laparoscopic group ($N=33$, 208 ± 55 minutes). Both groups had similar short-term outcomes. There were no differences in time to bowel function, pain scores, narcotic use, or time to bowel function. Conversion to open surgery was also significantly less for the hand-assisted group (2% versus 12.5%). Incision length was significantly longer for the hand-assisted group, but the difference was small (8.2 ± 1.5 versus 6.1 ± 2.1 cm). The authors concluded that hand-assisted surgery results in significantly shorter operative time, while maintaining similar outcomes as straight laparoscopic surgery.¹⁷

Recently, there has been a considerable debate about whether hand-assisted laparoscopic surgery is worthwhile. Straight and hand-assisted laparoscopic surgical techniques should not be mutually exclusive. Hand-assisted laparoscopic technique should be a part of armamentarium for all surgeons who perform laparoscopic colon surgeries. It may allow experienced surgeons

to complete more complex cases in a shorter amount of time.¹⁸

Long-Term Outcomes

All of the large prospective randomized trials presented their 3-year follow-up data.^{3,5,19,20} Recently two of these trials, the Barcelona and Clinical Outcomes of Surgical Therapy (COST) trials updated their results with 5-year follow-up data.^{2,4}

In 2008, Lacy et al reported an update on their long-term outcomes data from Barcelona trial.⁴ At that time, the median follow-up was 95 months (77–133). The overall survival rate was higher in the laparoscopic (64%) group when compared with the open group (51%), but the difference was not statistically significant ($p=0.07$). Similarly there was a trend toward higher cancer-related survival and lower cancer recurrence in the laparoscopic group ($p=0.07$ for both). As shown in their 3-year follow-up data, all of the differences in survival and recurrences between the two groups were observed in stage III patients. In stage III tumors, overall-survival ($p=0.048$), cancer-related survival ($p=0.02$), and chances of being free of recurrence ($p=0.048$) were significantly higher in the laparoscopic group. There were no such differences in the stage I or stage II patients. Based on these results, authors concluded that “in a dedicated laparoscopic center, LAC may result in a long-term survival benefit compared with OC, particularly in advanced cases. This oncological advantage can be explained by a preserved cellular immunity, attenuated stress and inflammatory response. These results are certainly intriguing and may represent what can be achieved oncologically after laparoscopic cancer surgery.

In 2007, Fleshman et al reported 5-year data from the COST study group trial. The 5-year data was available on 90% of patients who were followed. Unlike the Barcelona trial, there was no significant difference in the 5-year overall survival (laparoscopic surgery = 76.4%, open surgery = 74.6%), 5-year disease-free survival (laparoscopic surgery = 69.2%, open surgery = 68.4%), and recurrence rates (laparoscopic surgery = 19.4%, open surgery = 21.8%) between the two groups. There was also no significant difference in pattern of disease recurrence.²

In 2007, Bonjer et al reported a meta-analysis study based on 3-year follow-up database of the Barcelona, COST, COLOR and CLASICC trials. This study included 796 laparoscopic and 740 open surgery patients for analysis. They found no significant difference in 3-year overall survival, 3-year disease-free survival, or tumor recurrence rates between the two study groups. When results were stratified according to stages, there were no significant differences in survival between the two study groups.²¹

LAPAROSCOPY FOR RECTAL CANCER

There are many potential benefits to performing rectal surgery laparoscopically. Recent meta-analysis of studies of nonrandomized trials comparing laparoscopic versus open surgery showed the usual benefits associated with laparoscopy after laparoscopic rectal surgery for cancer: shorter time to bowel function and shorter length of stay.²² In addition, compared with open surgery, laparoscopy can provide unprecedented, unobstructed views of the rectal dissection planes even in a patient with a narrow pelvis, not only for the surgeon but to the entire surgical team. Magnified views of the surgical planes may allow more precise dissection. The pneumoperitoneum can also help open up the planes for mobilization of the mesorectum. Despite these potential advantages, adoption of laparoscopic rectal surgery has been limited for many reasons. Although there are now several prospective randomized trials demonstrating safety and benefits associated with laparoscopic colon cancer surgery, the same benefits have not yet been clearly demonstrated for laparoscopic rectal cancer surgery.²⁻⁵ In addition, concerns about inadequate oncologic rectal dissection, anastomotic complications, and technical challenges have limited the wide adaptation of laparoscopic rectal surgery.^{23,24}

There are many technical challenges that are associated with laparoscopic rectal cancer surgery.

One of the technical hurdles is obtaining adequate exposure by laparoscopically retracting the rectum. As one dissects down to the distal rectum, especially in patients with a narrow pelvis, crowding and clashing of instruments can result in poor exposure and inadequate dissection. For this reason, an experienced assistant is often required. The only prospective randomized trial comparing results of open versus laparoscopic surgery to include rectal cancer is the CLASICC trial.³ It reported a significantly increased positive circumferential margin following laparoscopic rectal cancer surgery (12%) when compared with similar patients in the open group (6%). This increase in positive radial margin may be related to difficulty in retraction and exposure.

A further challenge in laparoscopic rectal surgery is localization of the tumor. This is less of an issue when dealing with colon cancers because the lesions are easily identifiable with or without tattoo marks. This is not as easily accomplished with rectal cancers. Without tactile sensation it can be difficult to determine adequacy of distal rectal dissection and to be sure that the stapler is applied at the appropriate level distal to the tumor.

Limitations in current laparoscopic distal rectal stapling devices pose another set of challenges.

The current laparoscopic staplers roticulate to a maximum of 65 degrees, making horizontal division of the rectum difficult. For this reason, multiple firings are often required to complete distal rectal transection. For

low-lying lesions, this is less than ideal and may lead to increased anastomotic leakage. Morin et al reported a leak rate of 17% below 12 cm from the anal verge and as high as 25% in those who were not diverted following laparoscopic rectal surgery.²³ Leroy et al reported a similar leak rate of 20% in cancers below 15 cm following laparoscopic rectal surgery.²⁴ These reported leak rates are comparatively higher than those reported after open total mesorectal dissections (4–11%).^{25,26} Improvements in laparoscopic stapling technology may help circumventing this problem in the future.

Hybrid and Hand-Assisted Laparoscopic Rectal Surgery

In efforts to retain the benefits of laparoscopic surgery while not compromising oncologic rectal dissection, some have advocated performing hybrid procedures in which colonic portion of the surgery is performed using the “pure” laparoscopic technique and rectal dissection is performed open through a limited low midline or Pfannenstiel incision. Vithiananthan et al, in a retrospective review of 28 patients with rectal neoplasms who underwent sphincter-saving hybrid laparoscopic and open procedures, found a significant length of stay benefit was noted for this group when compared with a similar group of patients who underwent fully open procedures.²⁷

Alternatively, hand-assisted laparoscopic techniques can be used for rectal cancer surgery. In comparison to hybrid procedure where the incision is not created until the end of the procedure, the hand-assisted technique utilizes the incision from the very beginning by placing the hand into abdomen by using an access device through it. As shown in several studies, hand-assisted compared with a “straight” technique may result in a shorter operative time based on a colonic portion of the operation alone.^{17,18} High ligation of vessels, splenic flexure takedown, and lateral mobilization may be accomplished in a shorter period time with a hand-assisted technique.

In hand-assisted laparoscopic surgery, rectal exposure and dissection can be either performed directly through the incision using the open techniques or laparoscopically with manual assistance.²⁸ This allows us to take advantage of the unmatched laparoscopic view while performing oncologically equivalent exposure and dissection techniques as in open surgery. Hand-assisted laparoscopic surgery allows preservation of tactile sensation; therefore, it may circumvent the tumor localization problem associated with the “straight” laparoscopic technique. By performing distal rectal division directly through the incision using the open surgical staplers, hand-assisted laparoscopic rectal surgery may result in a lower anastomotic leakage rate. Currently, the Minimally Invasive Therapeutic Trials (MITT) group is close

to starting a multicenter randomized trial comparing “straight” versus hand-assisted laparoscopic proctectomy for rectal cancer.

Long-Term Outcomes

The United Kingdom Medical Research Council Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (UK MRC CLASICC) trial was one of the first multicenter randomized trials to include rectal cancer as a part of their study. Their initial reports of a high incidence of positive circumferential radial margins for laparoscopic group (12%), with its rate being twice as high as the open group’s (6%), raised serious concerns regarding safety of laparoscopic anterior resection for cancer.³ However, in their 3-year follow-up report this did not translate into an increase in the local recurrence rate. The open group’s local recurrence rate was 7.0% and the laparoscopic group’s was 7.8%. Similarly, there was no significant difference in the 3-year local recurrence rates between the laparoscopic (15.1%) and the open abdomino perineal resection (APR) (21.1%) groups. The overall disease-free survival rates were also equivalent between the two techniques for the patients who underwent anterior resection (laparoscopic surgery = 70.9%, open surgery = 70.4%) and APR (laparoscopic surgery = 49.8, open surgery = 46.9%).

In 2004, Leung et al initially reported a randomized study comparing laparoscopic and open resection for sigmoid, rectosigmoid, and rectal cancer.²⁹ An updated subgroup analysis of rectal cancer patients who underwent anterior resection showed that 5-year disease-free survival rates were similar between laparoscopic (83.7%) and open surgery (80.4%) groups.³⁰

In 2008, the same group reported their long-term results after laparoscopic versus open APR for low rectal cancers. This was a relative small single institution prospective randomized trial based on a 90-month follow-up of 99 patients. In this study, 3 of 51 (5.9%) laparoscopic and 2 of 48 (4.2%) open surgery patients had a positive circumferential radial margin. Local recurrence rate was observed in two laparoscopic (5%) and four open surgery (11.1%) group patients. The 5-year disease-free survival rates were also similar for the two groups: laparoscopic (78.1%) and open surgery (73.6%).³¹

In 2006, Aziz et al published results based on meta-analysis of 20 laparoscopic rectal cancer studies published between 1993 and 2004. This study included over 2000 subjects. They concluded that there was no significant difference between the laparoscopic and the open groups in terms of the positive circumferential radial margin and number of lymph nodes harvested.²²

Although these results are encouraging, we cannot make any conclusions about long-term outcomes

until we have results from adequately powered multicenter controlled trials. Currently, there are several ongoing multicenter trials that will hopefully provide us with answers in the near future: the American College of Surgeons Oncology Group (ACOSOG) Z6051 trial from the U.S.; the COLOR II trial from Europe, Canada, and Asia; and the Japanese Japan Clinical Oncology Group (JCOG) 0040 trial.

SUMMARY

Laparoscopic colon surgery for cancer has become the gold standard. Laparoscopic colon resection for cancer, in experienced hands, can be performed safely and reliably with many short-term benefits to the patients while resulting in at least equivalent long-term outcomes as open surgery. Other potential, but less conclusively demonstrated benefits include better preservation of cell-mediated immune function and reduced tumor cell proliferation. Although a similar level of evidence does not yet exist for the laparoscopic rectal surgery for cancer, the evidence to date suggests that it is likely that the ongoing large randomized trials will demonstrate clinical benefits of laparoscopic rectal cancer surgery.

REFERENCES

- Berends FJ, Kazemier G, Bonjer HJ, Lange JF. Subcutaneous metastases after laparoscopic colectomy. *Lancet* 1994; 344(8914):58; (Letter)
- Fleshman J, Sargent DJ, Green E, et al; for The Clinical Outcomes of Surgical Therapy Study Group. Laparoscopic colectomy for cancer is not inferior to open surgery based on 5-year data from the COST Study Group trial. *Ann Surg* 2007;246(4):655-662; discussion 662-664
- Jayne DG, Guillou PJ, Thorpe H, et al; UK MRC CLASICC Trial Group. Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC Trial Group. *J Clin Oncol* 2007; 25(21):3061-3068
- Lacy AM, Delgado S, Castells A, et al. The long-term results of a randomized clinical trial of laparoscopy-assisted versus open surgery for colon cancer. *Ann Surg* 2008;248(1):1-7
- Buunen M, Veldkamp R, Hop WC, et al; Colon Cancer Laparoscopic or Open Resection Study Group. Survival after laparoscopic surgery versus open surgery for colon cancer: long-term outcome of a randomised clinical trial. *Lancet Oncol* 2009;10(1):44-52
- Heald RJ, Moran BJ, Ryall RD, Sexton R, MacFarlane JK. Rectal cancer: the Basingstoke experience of total mesorectal excision, 1978-1997. *Arch Surg* 1998;133(8):894-899
- Southall JC, Lee SW, Allendorf JD, Bessler M, Whelan RL. Colon adenocarcinoma and B-16 melanoma grow larger following laparotomy vs. pneumoperitoneum in a murine model. *Dis Colon Rectum* 1998;41(5):564-569
- Allendorf JDF, Bessler M, Kayton ML, et al. Increased tumor establishment and growth after laparotomy vs laparoscopy in a murine model. *Arch Surg* 1995;130(6): 649-653
- Lee SW, Feingold DL, Carter JJ, et al. Peritoneal macrophage and blood monocyte functions after open and laparoscopic-assisted colectomy in rats. *Surg Endosc* 2003; 17(12):1996-2002
- Martin JK Jr, Goellner JR. Abdominal fluid cytology in patients with gastrointestinal malignant lesions. *Mayo Clin Proc* 1986;61(6):467-471
- Shantha Kumara HM, Feingold D, Kalady M, et al. Colorectal resection is associated with persistent proangiogenic plasma protein changes: postoperative plasma stimulates in vitro endothelial cell growth, migration, and invasion. *Ann Surg* 2009;249(6):973-977
- Veldkamp R, Khury E, Hop WC, et al. Colon Cancer Laparoscopic or Open Resection Study Group (COLOR). Laparoscopic surgery versus open surgery for colon cancer; short-term outcomes of a randomized trial. *Lancet Oncol* 2005;6:477-484
- Law WL, Lee YM, Choi HK, Seto CL, Ho JW. Impact of laparoscopic resection for colorectal cancer on operative outcomes and survival. *Ann Surg* 2007;245(1):1-7
- Lee SW, Gleason NR, Bessler M, Whelan RL. Port site tumor recurrence rates in a murine model of laparoscopic splenectomy decreased with increased experience. *Surg Endosc* 2000;14(9):805-811
- Hughes ESR, McDermott FT, Polglase AL, Johnson WR. Tumor recurrence in the abdominal wall scar tissue after large-bowel cancer surgery. *Dis Colon Rectum* 1983;26(9): 571-572
- Milsom JW, Böhm B, Hammerhofer KA, Fazio V, Steiger E, Elson P. A prospective, randomized trial comparing laparoscopic versus conventional techniques in colorectal cancer surgery: a preliminary report. *J Am Coll Surg* 1998; 187(1):46-54; discussion 54-55
- Marcello PW, Fleshman JW, Milsom JW, et al. Hand-assisted laparoscopic vs. laparoscopic colorectal surgery: a multicenter, prospective, randomized trial. *Dis Colon Rectum* 2008;51(6):818-826
- Lee SW, Yoo J, Dujovny N, Sonoda T, Milsom JW. Laparoscopic vs. hand-assisted laparoscopic sigmoidectomy for diverticulitis. *Dis Colon Rectum* 2006;49(4):464-469
- Lacy AM, García-Valdecasas JC, Delgado S, et al. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. *Lancet* 2002;359(9325):2224-2229
- Clinical Outcomes of Surgical Therapy Study Group. A comparison of laparoscopically assisted and open colectomy for colon cancer. *N Engl J Med* 2004;350(20): 2050-2059
- Bonjer HJ, Hop WC, Nelson H, et al; Transatlantic Laparoscopically Assisted vs Open Colectomy Trials Study Group. Laparoscopically assisted vs open colectomy for colon cancer: a meta-analysis. *Arch Surg* 2007;142(3): 298-303
- Aziz O, Constantinides V, Tekkis PP, et al. Laparoscopic versus open surgery for rectal cancer: a meta-analysis. *Ann Surg Oncol* 2006;13(3):413-424
- Morino M, Parini U, Giraudo G, Salval M, Brachet Contul R, Garrone C. Laparoscopic total mesorectal excision: a consecutive series of 100 patients. *Ann Surg* 2003;237(3): 335-342
- Leroy J, Jamali F, Forbes L, et al. Laparoscopic total mesorectal excision (TME) for rectal cancer surgery: long-term outcomes. *Surg Endosc* 2004;18(2):281-289

25. Enker WE, Thaler HT, Cranor ML, Polyak T. Total mesorectal excision in the operative treatment of carcinoma of the rectum. *J Am Coll Surg* 1995;181(4):335-346
26. Heald RJ, Moran BJ, Ryall RD, Sexton R, MacFarlane JK. Rectal cancer: the Basingstoke experience of total mesorectal excision, 1978-1997. *Arch Surg* 1998;133(8):894-899
27. Vithianathan S, Cooper Z, Betten K, et al. Hybrid laparoscopic flexure takedown and open procedure for rectal resection is associated with significantly shorter length of stay than equivalent open resection. *Dis Colon Rectum* 2001;44(7):927-935
28. Lee SW, Sonoda T, Milsom JW. Expediting of laparoscopic rectal dissection using a hand-access device. *Dis Colon Rectum* 2007;50(6):927-929
29. Leung KL, Kwok SP, Lam SC, et al. Laparoscopic resection of rectosigmoid carcinoma: prospective randomised trial. *Lancet* 2004;363(9416):1187-1192
30. Ng SS, Leung KL, Lee JF, Yiu RY, Li JC. MRC CLASICC trial. *Lancet* 2005;366(9487):713; author reply 713-714
31. Ng SS, Leung KL, Lee JF, et al. Laparoscopic-assisted versus open abdominoperineal resection for low rectal cancer: a prospective randomized trial. *Ann Surg Oncol* 2008;15(9):2418-2425