Laparoscopy for Colon and Rectal Cancer

Govind Nandakumar, M.D.,¹ and James W. Fleshman, M.D.¹

ABSTRACT

Laparoscopy has emerged as a useful tool in the surgical treatment of diseases of the colon and rectum. Specifically, in the application of colon cancer, a laparoscopic-assisted approach offers short-term benefits to patients while maintaining a long-term oncologic outcome. Hand-assisted laparoscopic surgery may help decrease operative times while preserving the benefits of laparoscopy. The literature on the use of laparoscopy for rectal cancer is still in its early stages. Limited data suggest short-term benefits without compromising oncologic outcome; however, data from large multicenter trials will clarify the role of laparoscopy in the treatment of rectal cancer. Robotic proctectomy is a novel technique that may offer considerable advantage and overcome some limitations laparoscopy creates while working in the confines of the pelvis. The improved magnification and visualization offered with the robot may also assist in preserving bladder and sexual function. Transanal endoscopic microsurgery (TEM) for the treatment of T1 rectal cancers with low-risk features appears to be safe. However, TEM has a significantly higher recurrence rate when used to treat invasive cancer. Endoluminal techniques and equipment are under development and could offer more minimally invasive approaches to the treatment of colon and rectal cancer. Credentialing and training of surgeons and teams involved in the use of laparoscopy is important prior to making these techniques ubiquitous.

KEYWORDS: Colon cancer, rectal cancer, laparoscopy

Objectives: On completion of this article, the readers should be able to summarize the current evidence supporting the use of laparoscopy for colon cancer and the use of laparoscopy, robotics, and transanal techniques for the treatment of rectal cancer.

Following the success and wide implementation of laparoscopic cholecystectomy, reports on the use of laparoscopy for colon resections soon appeared.¹ Unfortunately, due to initial concerns regarding the oncologic quality of the operation and reports of port site implants, there was hesitance in the application of laparoscopy to colon and rectal cancer. Between 1994 and 2004 there were multiple randomized control trials conducted to study the use of laparoscopy for the treatment of colon cancer.² The data on colon

cancer has since matured suggesting that laparoscopy offers short-term benefits with no compromise on the oncologic outcome. Evidence on the use of laparoscopy for rectal cancer is limited and we await the results of large multicenter randomized control trials to define the role of laparoscopy. This review aims to provide the current evidence for the minimally invasive management of colon and rectal cancer. We also highlight some of the upcoming technologies related to the application of robotic proctectomy, transanal

¹Section of Colon and Rectal Surgery, Washington University School of Medicine, St. Louis, Missouri.

Address for correspondence and reprint requests: Govind Nandakumar, M.D., Section of Colon and Rectal Surgery, Washington University School of Medicine, 660 South Euclid Ave, Box 8109, St. Louis MO 63110 (e-mail: doctorgovind@gmail.com).

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Table 1 Multicenter Trials and Meta-analyses on Laparoscopy for Colon Cancer

Study	# of Patients Lap	# of Patients Open	Outcomes
Randomized Multicenter Trial			
<i>COST</i>			
Weeks (2002) ^{8a}	215	213	Recovery
Nelson (2004) ^{8,9}	437	435	Recovery, 3 yr onc
Fleshman et al (2007) ³	437	435	5 yr onc
<i>COLOR I</i>			
Veldkamp et al (2005) ⁴	627	621	Recovery
Buunen et al (2009) ¹⁸	627	621	3 yr onc
<i>CLASICC</i>			
Guillou et al (2005) ⁵	273	140	Recovery
Jayne et al (2007) ⁶	273	140	3 yr onc
<i>ALCCaS</i>			
Hewett (2008) ⁷	294	298	Recovery
<i>Meta-analyses of Randomized Trial</i>			
Tjandra et al (2006) ¹⁰	2078	1935	Recovery
Bonjer et al (2007) ¹⁴	796	740	3yr onc
Jackson (2007) ^{9a}	859	835	1.5–5 yr onc

Lap, laparoscopy; Open, open surgery, onc, oncologic follow-up; COST, Clinical Outcomes of Surgical Therapy Study Group; COLOR I, Colon Cancer Laparoscopic or Open Resection I; CLASICC, Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer; ALCCaS, Australasian Randomized Clinical Study Comparing Laparoscopic and Conventional Open Surgical Treatments for Colon Cancer Trial.

endoscopic microsurgery, and endoluminal approaches to colon and rectal cancer.

COLON CANCER

In the late 1990s several large series showed that laparoscopy was feasible in the treatment of colon cancer.² Three large multicenter randomized control trials have looked at this topic—the Clinical Outcomes of Surgical Therapy Study Group (COST),³ Colon Cancer Laparoscopic or Open Resection I (COLOR I),⁴ and Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (CLASICC)^{5,6} trials (Table 1). More recently, short-term data from the Australasian Randomized Clinical Study Comparing Laparoscopic and Conventional Open

Surgical Treatments for Colon Cancer Trial (ALCCaS) echoed the findings of the other trials.⁷ Our discussion is limited to the large multicenter trials and meta-analysis of single-center randomized control trials.

Short-Term Outcomes

The three large multicenter trials revealed no difference in 30-day mortality or overall morbidity between laparoscopic-assisted or open surgery for colon cancer (Table 2). The two approaches had very similar short-term morbidity and had no difference in parameters of postoperative recovery. Specifically, there was no difference in the number of days to first bowel movement or postoperative length of stay.^{4,5,8,9}

Table 2 Short-Term Outcome on Laparoscopy for Colon Cancer

		COST	COLOR	CLASICC	ALCCaS
# Patients randomized (n)	Lap	437	627	273	294
	Open	435	621	140	298
1 st bowel movement (days)	Lap	3 (2–4)	3.6 (1.7)	5 (4–7)	4.4 (2.3–6.5)
	Open	4 (3–5)	4.6 (3.0)	6 (4–7)	4.9 (2.7–7.1)
Postoperative length of stay (days)	Lap	5 (4–6)	8.2 (6.6)	9 (7–12)	9.5 (2.1–16.9)
	Open	6 (5–7)	9.3 (7.3)	9 (8–13)	10.6 (3.4–17.9)
Overall 30-day morbidity (%)	Lap	21	21	26	39 (at least one complication)
	Open	20	20	27	45 (at least one complication)
30-day mortality (%)	Lap	0.5	1.1	4.0	1.4 (In-hospital)
	Open	0.9	1.8	4.9	.7 (In-hospital)

Lap, laparoscopy; Open, open surgery; COST, Clinical Outcomes of Surgical Therapy Study Group; COLOR I, Colon Cancer Laparoscopic or Open Resection I; CLASICC, Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer; ALCCaS, Australasian Randomized Clinical Study Comparing Laparoscopic and Conventional Open Surgical Treatments for Colon Cancer Trial.

A meta-analysis of randomized control trials that reported on short-term outcomes showed that significant early benefits measured as wound complications, intraoperative blood loss and narcotic use can be achieved with laparoscopy.¹⁰ The meta-analysis also noted a significantly shorter time to first bowel movement (23.9 hour difference) and discharge from hospital (1.7 days earlier). It is unclear why these differences were not obvious in the multicenter randomized control trials. The pooled number of patients that were included in the meta-analysis might have provided sufficient power to elucidate this difference. These results were consistent with the short-term data from the Australasian randomized clinical study comparing laparoscopic and conventional open surgical treatments for colon cancer trial. A significant decrease in the time to return of bowel function and the length of stay were noted in this trial.⁷ A Cochrane review of 25 randomized control trials cited improvements in intensity of pain, postoperative ileus, and 30-day quality of life scores with laparoscopy-assisted colon resections for cancer.¹¹

Oncologic Outcomes

During the early days of laparoscopic colorectal surgery, there was significant concern that there might be a higher incidence of port site metastasis with the use of laparoscopy. This concern has been laid to rest by good quality studies with 3- and 5-year survival data (Table 3). The COST Study Group presented 5-year follow-up data with no difference in disease-free survival or overall survival.³ Three-year oncologic data from the COLOR trial and a Cochrane data review also echoed these findings.^{12,13} An impressive meta-analysis pooled data on 3-year oncologic outcomes on overall and disease-free survival from the Barcelona, COST, COLOR, and CLASICC trials. Overall and disease-free survival were no different between the open and laparoscopically assisted colectomies.¹⁴

Lacy et al raised the question of possible oncologic benefit to laparoscopy.¹⁵ Data from this study showed a higher cancer-related survival in the laparoscopic group. Subgroup analysis showed that the difference was primarily seen in patients with stage III cancer. In experimental models, laparoscopy has the potential to inhibit the growth of intradermally injected cancer cells and decrease the establishment of pulmonary metastases.^{16,17} Unfortunately, these benefits have not been seen in the larger trials. Long-term follow-up of the current multicenter trials will clarify if laparoscopy has potential oncologic benefits.

Upcoming Trials

We look forward to the COLOR II and COST II data to clarify the long-term benefits of laparoscopy. Two international trials the Australasian randomized multicenter trial and the Japan Clinical Oncology Group (JCOG 0404) trial are awaited and will expand the data to include a more global perspective.¹⁸

Limitations

The exclusion criteria for these studies must be noted. Most large studies excluded patients with obstruction, stage IV disease, or cancers of the transverse colon. In the absence of data, the use of laparoscopy in these situations should be limited to experienced centers where data can be collected and reported in a systematic fashion.

It is important to understand the context of these studies and applicability of the findings. Most studies were conducted by experienced colorectal surgeons trained in open and laparoscopic cancer surgery working at specialized units. These results might not be matched by general surgeons working at community hospitals, performing low-volume colon cancer and laparoscopic surgery. Credentialing surgeons prior to beginning the trials served to standardize the operation. These

Table 3 Oncologic Data on Laparoscopy for Colon Cancer

		Overall Survival Rate (%)		Disease-Free Survival Rate (%)		Overall Recurrence Rate (%)	
Trial	Follow- up (Years)	Lap	Open	Lap	Open	Lap	Open
Multicenter Randomized Trials							
COST							
Nelson ^{8,9}	3	86	85	79.5	78	16	18
Fleshman et al ³	5	76.4	76.4	69.2	68.4	19.4	21.8
CLASICC							
Jayne et al ⁶	3	68.4	66.7	66.3	67.7	NA	NA
Meta-analyses of Randomized Trial							
Bonjer et al ¹⁴	3	82.2	83.5	75.8	75.3	14.2	16.4

Lap, laparoscopy; Open, open surgery; onc, oncologic follow-up; COST, Clinical Outcomes of Surgical Therapy Study Group; COLOR I, Colon Cancer Laparoscopic or Open Resection I; CLASICC, Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer.

standardized techniques can be transferred to all surgeons with an interest in treating colon cancer and the volume to learn the technique. Reports on community surgeon experience with laparoscopic colon surgery are emerging in the literature.^{19,20}

The techniques developed during these early trials have been standardized in definable steps, which are now used to teach residents, fellows, and fully trained practicing surgeons to perform a safe, oncologically sound colectomy for cancer.

Five Steps to Right Colon

1. Medial to lateral, lateral to medial, or posterior approach to mobilize the colon from the retroperitoneum
2. Release of hepatic flexure and exposure of duodenum
3. Incise the lateral attachments and omentum
4. Ligate vascular pedicles at the origin of the ileocolic and right colic vessels
5. Complete specimen extraction and anastomosis

Five Steps to Left Colon

1. Identification of the ureter following medial to lateral, lateral to medial, or cephalad to caudad approach
2. Isolation of the vascular pedicles: inferior mesenteric artery and vein at origin and first bifurcation
3. Medial or lateral mobilization of mesentery off the retroperitoneum
4. Detach lateral attachments and omentum, splenic flexure mobilization
5. Complete specimen extraction and anastomosis

Hand-Assisted Laparoscopy

The use of a hand-assist device during laparoscopic colon surgery mitigates some of the technical challenges of the procedure. Proponents of the hand-assist approach argue that since an extraction site is required for specimen removal, this incision can be used to facilitate dissection. Data from a multicenter randomized control trial showed shorter operative times, while maintaining the short-term benefits of laparoscopy for left and total abdominal colectomies.²¹ A single-center randomized control trial found no difference in the short-term outcome between straight laparoscopic and hand-assisted colectomy for cancer.²² A systematic review and meta-analysis that included colectomy performed for benign and malignant disease found no difference in the short-term outcome between laparoscopic and hand-assist surgery.²³ Hand-assisted laparoscopy is an important minimally invasive tool that aids in training new surgeons, expands the use of laparoscopy to

technically challenging cases that might have previously been approached without laparoscopy, and expedites the operation in the daily test of a busy surgeon.

RECTAL CANCER

The evidence for the use of laparoscopy in the setting of rectal cancer is limited when compared with colon cancer. Laparoscopic rectal surgery is more technically demanding than laparoscopic colon surgery. In the CLASICC trial, a randomized trial involving 27 centers in the United Kingdom, 242 rectal dissections were performed by surgeons who had completed a minimum of 20 laparoscopic colon resections. This specialized group of surgeons still had a conversion rate of 34% for rectal dissection. Tumor fixation and uncertainty of margins were the two most common reasons for conversion.⁵ A higher rate of positive radial margins after laparoscopic TME in patients who underwent sphincter-saving procedures was concerning. The higher incidence of positive margin did not affect 3-year survival or local recurrence rates compared with an open operation. In reviewing studies reporting on laparoscopic proctectomy for rectal cancer, it is critical to differentiate the “hybrid approach” (laparoscopic mobilization of the splenic flexure is followed by a TME via an “open” lower midline incision) from a laparoscopic TME (rectal dissection is performed laparoscopically). The “hybrid” operation follows the principles and technique of an “open” operation for the rectal dissection and would be expected to have similar results to an open approach. The CLASICC trial discussed earlier offers the highest level of evidence for the use of laparoscopy to treat rectal cancer.^{5,6} In addition, there are six other randomized control single institution trials looking at the application of laparoscopy for rectal cancer. These have all shown favorable outcomes for short-term results and oncologic parameters.

Short-Term Outcomes

In the CLASICC trial there was a decrease in median length of stay from 13 to 11 days with no significant difference in the time to first bowel movement and resumption of normal oral diet. Neither the meta-analyses nor the CLASICC trial reported any difference in 30-day mortality. The two meta-analyses showed more convincing short-term advantages including a lower incidence of wound infection (0% vs. 14%),²⁴ overall morbidity (21% vs. 28%)²⁵ return of stoma function (1.5 days earlier), and length of stay (2.7 days shorter) for the laparoscopic group.²⁴

Oncologic Outcomes

Total mesorectal excision (TME) has decreased the incidence of recurrence after proctectomy for rectal

cancer.^{26,27} Adherence to this principle with laparoscopic surgery seems critical in maintaining a good oncologic outcome. Best available markers for a successful TME remain evaluation of the quality of the TME specimen—circumferential resection margin (CRM), distal margin, and number of lymph nodes. The 2006 meta-analysis showed no difference in the oncologic data between laparoscopic and open approaches.²⁴ One concerning trend noted in the CLASICC trial was a numerically larger though statistically insignificant rate of positive circumferential margin (CRM) in laparoscopy assisted anterior resection (12% vs. 6%).⁵ Interestingly the rate of complete TME was higher in the laparoscopic group compared with the open group supporting the argument that laparoscopy might offer better visualization and magnification in the pelvis. In the meta-analyses, the rates of positive CRM were lower overall and not different between the laparoscopic and open groups.²⁴

A second marker of oncologic technique is the number of lymph nodes retrieved during TME. Two randomized controlled trials and other large non-randomized comparative trials found no difference in the number of lymph nodes retrieved between the laparoscopic and open rectal resections.^{28–33}

BLADDER AND SEXUAL FUNCTION

Preservation of pelvic nerves during TME is important to maintain bladder and sexual function. Despite efforts to identify and preserve pelvic nerves during TME, the incidence of bladder and sexual dysfunction has been reported to be 0 to 12% and 10 to 35%, respectively.^{34–36} The magnification offered with laparoscopic dissection may facilitate the identification of pelvic nerves.^{37,38} There is limited data to clarify if laparoscopy offers better identification of autonomic nerves. In the CLASICC trial data, bladder and sexual function was found to be no different between laparoscopic and open TME. Male sexual function and erectile function tended to be worse in the laparoscopic group compared with the open group though not statistically significant ($p = 0.063$). The authors attributed the difference to the higher number of TME dissections in the laparoscopic group.³⁵ Clearly, preservation of pelvic nerves is an important aspect of proctectomy and upcoming studies will clarify if laparoscopy will offer improved identification and preservation of pelvic nerves.

The CLASICC trial reported 3-year outcomes on local recurrence with no difference noted between the laparoscopic and open approaches. Although these results are encouraging and suggest that the open and laparoscopic techniques are equivalent, the data are rudimentary. The COLOR II trial, JCOG study 0404, Australian ALACART trial, and the American College of Surgeons Oncology Group trials Z6051 are underway and should provide good quality data on the oncologic

outcome on laparoscopy for rectal cancer. In the absence of 5-year survival data, laparoscopic proctectomy should be offered only in the setting of a trial. In an effort to collect data in a systematic fashion, the Society of American Colon and Rectal Surgeons (SACRS) and the Society of Gastrointestinal and Endoscopic Surgeons (SAGES) issued a joint statement encouraging surgeons to perform laparoscopic proctectomy for cancer in the setting of a trial.³⁹

ROBOTIC PROCTECTOMY

Operating within the confines of the pelvis to perform a good total mesorectal excision for cancer is technically demanding with the laparoscope. Robotic systems are useful when the operative field is small and a precise dissection is required to successfully complete the operation. There have been recent reports looking at the feasibility of robotic proctectomy for rectal cancer. Initial case series have reported short-term outcomes similar to laparoscopic proctectomy.^{40–42} Baik et al reported on 56 patients who underwent robotic proctectomy for rectal cancer. The conversion rate to open was 0% in the robotic group compared with 10% in the laparoscopic group with a higher number of “complete TME” in the robotic group. However, these trends were not statistically significant.⁴⁰ Robotic proctectomy may offer improved visualization of the pelvic nerves and decrease the rate of bladder and sexual dysfunction. Interestingly, laparoscopic surgeons who work in the pelvis commonly have lower back problems and robotic systems might create a more ergonomically friendly environment for the surgeon during proctectomy.⁴³ However, robotic proctectomy is a new technique under development and requires more rigorous studies prior to accepting its use as standard therapy for the treatment of rectal cancer. Robotic laparoscopic procedures are being included in the laparoscopic arm of the ACOSOG Z6051 trial.

TRANSANAL ENDOSCOPIC MICROSURGERY

Total mesorectal excision (TME) remains the gold standard for the treatment of rectal cancer.⁴⁴ However, the morbidity and mortality associated with the operation is considerable. Techniques for transanal excision of rectal adenomas and selected early rectal cancers have been developed. Transanal endoscopic microsurgery (TEM) offers improved visualization and expands the indications to include tumors located in the upper rectum. TEM is being used increasingly in the treatment of early rectal cancers.

The TEM experience with adenomas was recently reviewed by Middleton and included 55 case series and three comparative studies including a randomized control trial.⁴⁵ While recognizing the paucity of data, they concluded that TEM might offer lower recurrence rates compared with transanal excision for rectal adenomas.

TEM might prove to be a good option in the setting of a large rectal polyp that harbors an occult carcinoma.

TEM has also been used to treat low-risk T1N0 rectal adenocarcinoma with favorable prognostic factors. Retrospective data on long-term recurrence rates for T1 lesions have been reported to be 4 to 6% in the low-risk group versus 33 to 39% in the high-risk group.^{46,47} Five-year data from a randomized control trial that compared TEM and anterior resection showed no difference in 5-year survival with a significant ($p < 0.05$) difference in short-term benefits such as length of stay, blood loss, operative time, and analgesic requirements.⁴⁸ Similar case experiences have been reported by other authors.^{49–52} A rigorous, multicenter trial is required to study this topic; however, current available evidence suggests that low-risk T1 tumors can be treated with TEM. TEM is not a good option for T2 and T3 tumors as the recurrence rate can be as high as 50 to 66%.^{46,53} The role of TEM in conjunction with neoadjuvant chemoradiation therapy might expand the indications for TEM.⁵⁴

TEM and emerging endoluminal approaches to the management of colon and rectal malignancy are an exciting new frontier. We have successfully developed a cadaver model to perform a transanal proctectomy using TEM to establish entry into the pelvis for laparoscopic techniques through a single-port system at the anus.⁵⁵ TEM may also prove to be useful in palliating patients who might not be good candidates for an open approach.

TRAINING AND CREDENTIALING

Early literature reported the learning curve for laparoscopy to be 20 to 50 cases.^{56–58} The COST and CLASICC trials required a minimum of 20 cases and a reviewed validated video for surgeons to be credentialed to perform laparoscopic colon surgery.^{5,8} Extrapolating from the COST and CLASICC experience, the ASCRS and SAGES recommended 20 as the minimum number of laparoscopic colon resections to be credentialed.⁵⁹ Although 20 might serve as a minimum, the issue of credentialing is controversial and it is hard to recommend an absolute number. Participation in courses sponsored by organizations such as the American Society of Colon and Rectal Surgeons facilitates adoption of laparoscopic techniques in clinical practice.⁶⁰ Credentialing for laparoscopic proctectomy, robotic proctectomy, and NOTES will remain a challenge as these techniques develop. Efforts to standardize the surgical technique in these trials are important to provide good data encompassing two surgical procedures. Video credentialing and a random video audit can assure quality technique.

CONCLUSIONS

Laparoscopy is a safe and effective strategy in the treatment of colon cancer. Credentialing and training sur-

geons of the future is important to be able to reproduce the results of the large multicenter trials. Laparoscopy in the treatment of rectal cancer is still under investigation and should only be performed in the setting of a clinical trial. Robotic proctectomy is an emerging technique and may prove to be a good surgical option for the treatment of rectal cancer. Transanal endoscopic microsurgery and endoluminal approaches might offer important treatment options in the future.

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