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Evidence-based Series 2-20-2 EDUCATION AND INFORMATION 2011

Laparoscopic Surgery for Cancer of the Colon

A. Smith, R.B. Rumble, B. Langer, H. Stern, F. Schwartz, M. Brouwers, and members of Cancer Care Ontario's Laparoscopic Colon Cancer Surgery Expert Panel and Program in Evidence-based Care

A Quality Initiative of Cancer Care Ontario's
Surgical Oncology Program and the Program in Evidence-based Care

Report Date: September 2005

This Evidence-based Series (EBS) was reviewed in September 2011 and put in the Education and Information section in 2012. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol).

The reviewed report consists of:

Section 1: Clinical Practice Guideline

Section 2: Systematic Review

Section 3: Guideline Development and External Review

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Evidence-based Series #2-20-2: Section 1

Laparoscopic Surgery for Cancer of the Colon: A Clinical Practice Guideline

A. Smith, R.B. Rumble, B. Langer, H. Stern, F. Schwartz, M. Brouwers, and members of Cancer Care Ontario's Laparoscopic Colon Cancer Surgery Expert Panel and Program in Evidence-based Care

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This report provides clinical, professional, and organizational advice regarding the role of laparoscopic surgery for adult patients with stages I, II, or III colon cancer for whom surgery is the first-line treatment of choice. These recommendations are limited to patients for whom there is available evidence, who do not have colon cancer associated with perforation, obstruction, fistula or attachment to other structures (locally advanced). This report does not apply to patients with rectal cancer.

This advice document is intended to assist in clinical decision making and planning for ALL surgeons (general surgeons, colorectal surgeons, etc.) and ALL institutions that treat patients with colon cancer in the Province of Ontario, Canada.

PART ONE: CLINICAL ISSUES

Clinical Question

Can laparoscopic surgery be recommended as an alternative to conventional open surgery for patients with stages I, II, or III colon cancer (not rectal cancer) based on a comparison of outcomes? Primary outcomes of interest include survival, recurrence, and adverse event rates. Secondary outcomes of interest are operating time and time until hospital discharge.

Target Population

Adult patients with stage I, II, or III colon cancer (not rectal cancer).

- Who do not have perforation, obstruction, fistula, or attachment to other structures (locally advanced disease).

Clinical Recommendations

Based on the clinical evidence, a consensus of expert opinion, and the experience of members of the Laparoscopic Colon Cancer Surgery Expert Panel (LCCSEP), the following is recommended:

- Laparoscopic surgery is recommended as an acceptable option for the treatment of stage I, II, or III colon cancer and should be considered an alternative to conventional open surgery for colon cancer in specified patients.

Key Evidence

- Pooling data from two randomized controlled trials involving 1,071 patients did not detect a statistically significant difference between laparoscopic surgery and open surgery for survival (85% versus 83%, respectively).
- Pooling data from two randomized controlled trials involving 1,071 patients did not detect a statistically significant difference between laparoscopic surgery and open surgery for recurrence (17% versus 21%, respectively).
- Data analyses from four randomized controlled trials each detected a statistically significant difference between laparoscopic surgery and open surgery for operating times in favour of open surgery (unweighted mean across studies: 163 minutes versus 111.5, respectively).
- Data analyses from four randomized controlled trials each detected a statistically significant difference between laparoscopic surgery and open surgery for time to hospital discharge in favour of laparoscopic surgery (unweighted mean across studies: 5.1 days versus 7.3 days, respectively).

Qualifying Statements

- The patient population to whom this guideline applies was the standard population studied in the randomized controlled trial reviewed.
- These recommendations do not apply to patients with colon cancer associated with perforation, obstruction, fistula, or attachment to other structures (locally advanced disease).
- The recommendations do not apply to patients with rectal cancer as evidence is unavailable for this population.
- Possible contraindications to performing a laparoscopic colon resection include general contraindications applicable to colon surgery in general, those applicable to other laparoscopic procedures in general, or those specific to a subgroup of patients. Previous colon resection, significant obesity, or another major medical illness represent relative contraindications and should only be approached by experienced laparoscopic colorectal surgeons.

PART TWO: PROFESSIONAL PRACTICE ISSUES

Professional Practice Question

What is the recommended experience and training for surgeons who perform laparoscopic surgeries for cancer of the colon?

Professional Practice Recommendations

- The Laparoscopic Colon Cancer Surgery Expert Panel recommends that surgeons should have completed a number of laparoscopic colectomies to a level of accepted competence, as determined by their peers in a structured mentoring process. The best evidence available indicates that primary outcomes are not statistically different between laparoscopic and open surgery for colon cancer after at least one member of the team has performed 20 laparoscopic colon resections, for either benign or malignant disease. Therefore, it is

recommended that either this number be adhered to or an equivalent process, including peer evaluation, be undertaken.
- Surgeons are strongly encouraged to self-audit their experiences. The use of audit tools such as that championed by the Canadian Association of General Surgeons (CAGS) is recommended.

Key Evidence
While identifying the minimum number of procedures to achieve competency has not been the explicit subject of study, these standards reflect the best available evidence to date, which are the professional characteristics of surgeons in the Clinical Outcomes of Surgical Therapy (COST) study, the largest randomized trial of laparoscopic colon cancer resection performed to date. Both the American Society of Colon and Rectal Surgeons (ASCRS) and the Society of American Gastrointestinal Endoscopic Surgeons (SAGES) have endorsed similar recommendations. The opinion of the Laparoscopic Colon Cancer Surgery Expert Panel is that these standards reflect the best evidence currently available regarding the minimum training required to achieve acceptable outcomes in curable colon cancer.

PART THREE: INSTITUTIONAL AND ORGANIZATIONAL ISSUES
Institutional and Organizational Question
What are the recommended criteria for institutions performing laparoscopic surgeries for cancer of the colon?

Institutional and Organizational Recommendations
The Laparoscopic Colon Cancer Surgery Expert Panel recommends that all eligible institutions should show a commitment to advanced laparoscopic surgery by providing appropriate equipment, operating room time, and human resources, including developing a team approach to maximize the experience and efficiency of all team members.

Key Evidence
The Laparoscopic Colon Cancer Surgery Expert Panel agreed that optimal results in advanced laparoscopic surgery, including colon cancer, depend on a commitment to appropriate equipment and resources.

Future Research
New evidence available through studies presently underway and/or the evolution of technology may change these recommendations in the future, and the results of ongoing trials will be integrated into updates of this document.

Related Guidelines
- Practice Guideline Report #2-1: *Adjuvant therapy for stage II colon cancer following complete resection*.
- Practice Guideline Report #2-2: *Adjuvant therapy for stage III colon cancer following complete resection*.
- Practice Guideline Report #2-20-1: *Mesorectal excision for rectal cancer [in progress]*.

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The PEBC is supported by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from its funding agencies.

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Evidence-based Series #2-20-2: Section 2

Laparoscopic Surgery for Cancer of the Colon: A Systematic Review

A. Smith, R.B. Rumble, B. Langer, H. Stern, F. Schwartz, M. Brouwers, and members of Cancer Care Ontario's Laparoscopic Colon Cancer Surgery Expert Panel and Program in Evidence-based Care

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Report Date: September 2005

QUESTIONS

Can laparoscopic surgery be recommended as an alternative to conventional open surgery for patients with stages I, II, or III colon cancer (not rectal cancer) based on a comparison of outcomes? Primary outcomes of interest include survival, recurrence, and adverse event rates. Secondary outcomes of interest are operating time and time until hospital discharge.

Considering the available evidence, what are the optimum professional practice standards and institutional and organizational standards that would support best practice?

INTRODUCTION

The incidence rates of colorectal cancer in Ontario are in a state of transition. For males, incidence rates rose until 1984, plateaued, and then declined by an average 1% per annum between 1987 and 1996 (1). For females, incidence rates rose until 1979, plateaued, and then declined an average of 1.6% per annum between 1982 and 1996 (1). Colorectal cancer is the fourth most common cancer site in both sexes combined (13.1% of all new cancer cases) (1). In males, colorectal cancer is the third most common site, representing 13.3% of all new diagnoses, and in females, colorectal cancer is the second most common site, representing 12.9% of all new cases (1).

Mortality rates have also been on the decline for both men and women since 1971 (1). Despite this, colorectal cancer is the second leading cause of cancer death in both sexes combined (10.6% of all cancer deaths) (1). For both males and females, colorectal cancer ranked third as the leading cause of death, after breast and lung in females, and after lung and prostate in males (1). For that reason, there is great interest in improving the treatment results for this group of patients.

For colon cancer, en bloc surgical resection is the standard first-line treatment (2). This involves the removal of a portion of non-cancerous colon tissue both proximal and distal to the tumour, with adequate lateral margins (if the tumour is adherent to a continuous structure), and the removal of regional lymph nodes (2). Past studies have indicated that a resection margin of

5cm is adequate (2). In addition, the potential curative outcome of colon cancer surgery is determined not only by the complete removal of the tumour en bloc but also by an accompanying lymphadenectomy (2). The current recommendations are that a minimum of 12 lymph nodes be assessed to optimize the chances for accurate staging and to inform decision making regarding adjuvant treatment. Depending on the stage of the resected tumour, adjuvant treatment may be offered to patients in an attempt to eradicate any micro-metastases, which could otherwise lead to cancer recurrence.

Currently, two surgical procedures exist for the excision of colon cancers, conventional open surgery (CON) and laparoscopic surgery (LAP). In the LAP procedure, the tumour is excised, either extracorporeally through a small incision or within the abdomen, and removed (2). Preliminary trials reported many benefits of surgical excision using the LAP method, including: shorter hospital stays, reductions in stress and immunosuppression (2), reduced postoperative pain, earlier recovery of bowel function, and earlier return to normal activities. Those same preliminary reports also hypothesized that LAP may carry the following harms: improper tissue manipulation may lead to tumour dissemination, the wrong segment of colon may be removed because the surgeon is unable to palpate the tissue prior to resection, and use of the LAP tocars may result in port-site tumour implants resulting in recurrence (even in the absence of lymph node metastases or abdominal seeding) (2).

In the past, laparoscopic surgery for colon cancer was rarely performed outside of clinical trials. As more data become available, however, more surgeons are performing laparoscopic surgeries for the curative resection of colon cancer. Currently, a province-wide survey of general surgeons is taking place to assess current surgical practice for curable colon cancer. The results of another survey, in which 103 hospitals participated in a structured interview process (90% response rate) (unpublished data from trial by lead author AS), helped to inform the content of this report.

The objective of this report is to perform a systematic review of the evidence comparing the risks and benefits of LAP versus CON and to develop a set of evidence-based recommendations to inform clinicians, patients, and institutions (hospitals, universities, etc.).

METHODS

Guideline Development

This systematic review was developed by the Laparoscopic Colon Cancer Surgery Expert Panel (LCCSEP) as a collaborative project between two Cancer Care Ontario programs, the Surgical Oncology Program (SOP) and the Program in Evidence-based Care (PEBC). Clinicians from the SOP and the community, along with methodologists from the PEBC developed this report using the methods of the Guidelines Development Cycle (3).

Feedback and participation by Gastrointestinal Cancer Disease Site Group (DSG) members followed and informed the current draft being circulated to Ontario stakeholders.

Evidence was selected by and reviewed by one clinician (AS) and one methodologist (RBR) of the LCCSEP.

This systematic review is a convenient and up-to-date source of the best available evidence on laparoscopic surgery for colon cancer. The body of evidence in this review is primarily comprised of mature randomized controlled trial data. This evidence forms the basis of a clinical practice guideline developed by the members of Cancer Care Ontario's LCCSEP. The systematic review and companion practice guideline are intended to promote evidence-based practice in Ontario, Canada. The panel is supported by and editorially independent of Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

Literature Search Strategy

The MEDLINE (1985 to July week 4 2004), CANCERLIT (1986 to March 2001) and Cochrane Library's Evidence-based Systematic Reviews (through 2004, Issue 2) databases were searched using the Medical Subject Headings *colonic neoplasms/surgery* and the keywords *cancer* and *colon* both combined with the keyword *laparoscopy*. Ongoing clinical trials were identified using the National Cancer Institute (NCI) database on the Internet (http://www.cancer.gov/search/clinical_trials/). Relevant articles were selected and reviewed by two reviewers, and the reference lists from those sources were searched for additional trials. The reference lists from review articles were also searched for relevant evidence.

Study Selection Criteria

Eligible Studies

1. Randomized controlled trials (RCTs) comparing laparoscopic colon surgery to conventional open surgery.
2. Systematic Reviews (including meta-analyses and practice guidelines).
3. Papers published in English only.

Exclusion Criteria

1. In the trials, the majority of patients were treated for conditions other than cancer, or the proportion of colon or rectal cancer patients was not clearly described or indicated.
2. Abstracts.
3. Letters and editorials describing trial results.

Synthesizing the Evidence

As the results were obtained from fully published trial reports, individual patient data were not available for review. All the primary outcomes (overall survival, recurrence, and adverse event rates) could be synthesized via meta-analysis. For each comparison, the number of patients randomized to each treatment arm was used as the denominator, except where only the number of evaluable patients was provided. Survival data were pooled at the reported time of follow-up, which varied across trial reports. Combining data this way assumes a constant hazard of risk within the groups being compared over time; however this assumption was not tested. Data were pooled using the meta-analysis software package Review Manager (RevMan version 4.2.1, 9 April 2003) (The Cochrane Collaboration, Oxford, England). Results are expressed as the relative risk ratio (RR), where an RR < 1 favours the treatment group, and an RR > 1 favours the control group. Data were analyzed using the random effects model as the more conservative estimate of effect (4), and expressed with a 95% confidence interval (CI). Insufficient data were available to allow for appropriate pooling of the secondary outcomes (operating times and time until hospital discharge); ranges and overall unweighted means are reported. Weighted means could not be properly calculated because standard deviations were not reported in the studies.

RESULTS

Literature Search Results

A total of five (5-9) fully published RCT reports met our criteria and form the body of evidence for this report. No systematic reviews, meta-analyses, or clinical practice guidelines were found.

Quality of the Evidence Reviewed

All five of the trials obtained (5-9) were described as being randomized, and three (7-9) described the method of randomization. Two of the trials (7,8) stated that the end analysis was completed using the intent-to-treat principle. None of the trials mentioned blinding.

Outcomes

A summary of the RCT data appears in Table 1.

Table 1. Randomized Controlled Trials included in the practice guideline report.

Study (ref)	Type	Patients (n) [eval]	Conv. Rate %	Mean Duration of surgery (minutes)	Length of hospital stay (days)	Mean Lymph nodes removed (n)	Postop. Comp.† % [Table 2]	Median follow-up (years)	Recurrence %*	Overall Survival %*
Stage et al 1997 [5]	LAP	18 [15]	17	150	5	7	0	1.16	NR	NR
	CON	16 [14]		95	8	8	0			
Curet et al 2000 [6]	LAP	25	28	210	5.2	11	5	4.9	0	NR
	CON	18		138	7.3	10	28		6	NR
Hazelbroek et al 2002 [7]	LAP	NR	16.7	NR	NR	NR	NR	NR	NR	NR
	CON	NR		NR	NR	NR	NR		NR	NR
Lacy et al 2002 [8]	LAP	111 [106]	11	142	5.2	11.1	11	3.6	17	82
	CON	108 [102]		118 p=0.001	7.9 p=0.005	11.1	29 p=0.001		27 p=0.07	74 p=0.14
COST Study Trialists 2004 [9]	LAP	435	21	150	5	12	19	4.4	17.4	86
	CON	428		95 p<0.001	6 p<0.001	12	19		19.6	85 p=0.51

* Calculated at time of follow-up. Follow-up times varied across studies.

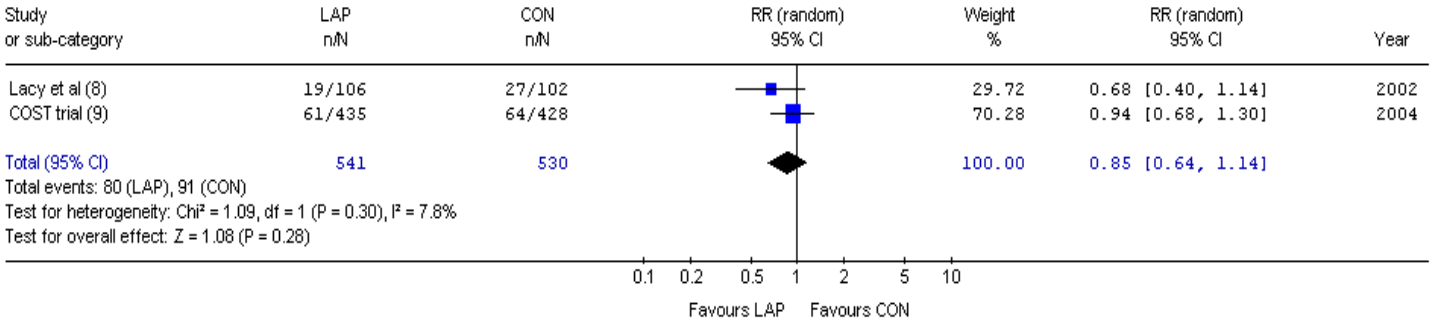
† As reported in the trial reports, which varied across studies.

Note: Conv. Rate, conversion rate from LAP to CON; CON, conventional open surgery; LAP, laparoscopic surgery; NR, not reported; COST, Clinical Outcomes of Surgical Therapy.

Survival

Only two trials provided data on overall survival (8,9). The trial by Lacy et al (8) reported survival at five years, and the COST trial (9) reported survival at three years. Pooling the data (Fig. 1) did not detect a statistically significant difference between laparoscopic surgery (85.2%) and open surgery (82.8%) for survival (RR=0.85 (95%CI, 0.64, 1.14; p=0.28)), and no statistical heterogeneity was detected (p=0.30).

Figure 1. Overall survival by treatment arm: laparoscopy versus open surgery.

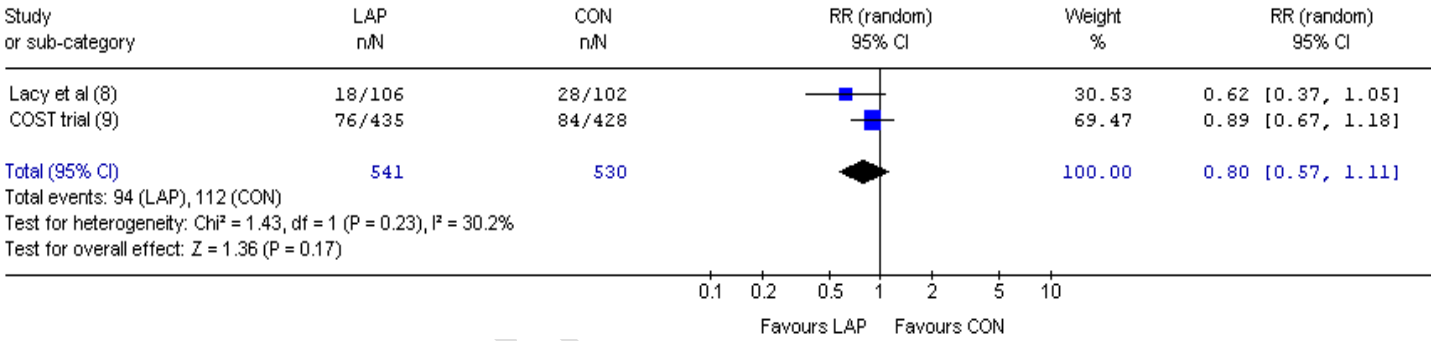


RR=0.85 (95%CI, 0.64, 1.14; p=0.28)

Recurrence

Two trials provided poolable data on recurrence (8,9). Pooling the data (Fig. 2) did not detect a statistically significant difference between laparoscopic surgery (17.4%) and open surgery (21%) for recurrence (RR=0.80; 95%CI, 0.57, 1.11; p=0.17), and no statistical heterogeneity was detected (p=0.23).

Figure 2. Recurrence by treatment arm: laparoscopy versus open surgery.



RR=0.80 (95%CI, 0.57, 1.11; p=0.17)

Adverse Events

Three (6,8,9) of the five trials provided poolable data on adverse events. These events were not graded; the numbers pooled were the actual number of events reported in each trial. The trial by Stage et al (5) did not report adverse events by treatment arm, and no adverse events were reported by Hazelbroek et al for the COLOR trial (7). A summary of adverse event data appears in Table 2. A pooled analysis was planned where the number of adverse events reported in each treatment arm was compared. Pooling the data did not detect a statistically significant difference between laparoscopic surgery and open surgery for the incidence of adverse events RR=0.52 (95%CI, 0.19, 1.37; p=0.18) (Figure not shown). Significant statistical heterogeneity was detected in this comparison (p=0.002), but interpretation was not affected as the outcome was not significant.

Table 2. Adverse events.

Study (ref)	Description	
Stage et al 1997 [5]	• Laparoscopic patients reported less pain at rest (p<0.01), during coughing (p<0.05), and during mobilization post-surgery (p<0.05). • Laparoscopic patients in group one suffered less pain at rest throughout the study period. • One patient in the laparoscopic group developed pneumonia and esophagitis.	
Curet et al 2000 [6]	Laparoscopic treatment arm: • Wound infection – 6%	Conventional open surgery treatment arm: • Wound infection – 6% • Bowel obstruction – 6% • Pneumonia – 6% • Cardiac event – 6% • Deep vein thrombosis – 6%
Lacy et al 2002 [8]	Laparoscopic treatment arm: • Wound infection rate 7% • Persistent ileus – 2.7% • Acute renal failure – 1.8%	Conventional open surgery treatment arm: • Wound infection rate - 17% • Persistent ileus – 8% • Evisceration – 1.9% • Intraperitoneal hemorrhage - <1% • Intraluminal hemorrhage - <1% • Anastomotic leak – 1.9% • Intraabdominal collection - <1% • Acute renal failure - <1% • Hepatic cirrhosis – 1.9%

COST Study Trialists 2004 [9]	Laparoscopic patients had briefer use of narcotics (p<0.001) and oral analgesics (p<0.02).
	There was no significant difference between the groups in:
	• Complications
	  • Overall complications: 20% CON versus 21% LAP; p=0.64
	  • Intraoperative complications: 2% CON versus 4% LAP; p=0.10
	  • Postoperative complications: 19% CON versus 19% LAP; p=0.98
	• 30-day postoperative mortality (p=0.40)
	• Rates and severity of postop complications at discharge (p=0.98) and at 60 days (p<0.73).
	• Rates of readmission (12% versus 10%; p=0.27)
	• Rates of reoperation (<2% versus <2%; p<1.0)	

Operating Time

A total of four trials reported on mean operating times (5,6,8,9). Across each of the four studies, statistically significant differences between laparoscopic surgery (range:142 to 210 minutes) and conventional open surgery (range 95 to 138 minutes) were found, with open surgery having significantly shorter operating times (overall unweighted means: LAP = 163 minutes versus CON = 111.5 minutes).

Time to Hospital Discharge

A total of four trials reported on mean time to hospital discharge (5,6,8,9). Across each of the four studies, statistically significant difference between laparoscopic surgery (range: 5.0 to 5.2 days) and conventional open surgery (range: 6.0 to 8.0 days) were found, with laparoscopic surgery having significantly faster times to hospital discharge (overall unweighted means: LAP = 5.1 days versus CON = 7.3).

Table 3. Physician's laparoscopic surgical experience by study.

Study (ref)	**Description of surgeons experience with laparoscopic techniques.**
Curet et al 2000 [6]	Trial report notes that all surgery was performed by attending physicians and residents, who had all performed multiple laparoscopically assisted colectomies for benign disease and palliation. All surgeries performed were supervised.

Hazelbroek et al 2002 [7]	Trial report notes that at least one member of the operating team had to have experience with 20 or more procedures. Standardization of laparoscopic technique was done by showing live and computerized demonstrations of laparoscopic resections to participating surgeons.
Lacy et al 2002 [8]	Trial report notes that both laparoscopic and conventional surgeries were performed by an experienced gastrointestinal team, but what qualified as experienced was not defined.
COST Study Trialists 2004 [9]	Trial report notes that each surgeon has performed at least 20 laparoscopic procedures prior to trial start. All potential surgeons submitted a videotape of themselves performing a laparoscopic procedure, and were assessed on the basis of the following criteria: • Level of mesenteric ligation • Degree of avoidance of direct handling of the tumour • Identification of critical adjacent structures • Thoroughness of abdominal exploration Ongoing quality control was done through random audits of videotaped procedures and examination of bowel margins. All were externally reviewed by a monitoring committee.

Table 4. Patient profile by study.

Study (reference)	Patient characteristics
Stage et al 1997 [5]	Age range (years): 61-93 (laparoscopic patients); 48-87 (CON patients) Contraindications to laparoscopic surgery: • Preoperative signs of extensive tumour growth • Patients scheduled for low anterior resection or abdominoperineal resection
Curet et al 2000 [6]	Age range (years): 45-83 (laparoscopic patients); 49-82 (CON patients) Contraindications to laparoscopic surgery: • Undergoing colostomy placement or removal • Complete or near complete colon obstruction resulting insignificant proximal distention • Presence of malignant fistualization or fixation in adjacent tissues
Hazelbroek et al 2002 [7]	Mean age: 70 (all patients) Contraindications to laparoscopic surgery: • Metastases • Previous or synchronous or previous malignancies (excluding skin and cervical cancers) • Obesity • Acute intestinal obstruction • Pregnancy
Lacy et al 2002 [8]	Age range (years): 56-80 (laparoscopic patients); 60-82 (CON patients) Contraindications to laparoscopic surgery: • Cancer located in the transverse colon • Distant metastases • Adjacent organ invasion • Intestinal obstruction • Past colon surgery

COST Study Trialists 2004 [9]	Age range (years): 28-96 (laparoscopic patients); 29-94 (CON patients) Contraindications to laparoscopic surgery: • Advanced local or metastatic disease • Cancer located in the transverse colon • Acute bowel obstruction • Bowel perforation from cancer • Inflammatory bowel disease • Familial polyposis • Synchronous or previous malignancies • Other severe medical illness

DISCUSSION

Analysis of the evidence obtained from five RCTs comparing laparoscopic surgery to open surgery for colon cancer detected no statistically significant difference between the groups for overall survival, recurrence, and adverse effects but studies consistently reported statistically significant differences between the groups for operating time (in favour of open surgery) and time to hospital discharge (in favour of laparoscopic surgery).

Based on the review of that evidence, the LCCSEP concluded that many patients would choose laparoscopic surgery over open surgery for colon cancer due to the more favourable time to hospital discharge, which does not negatively affect survival or disease recurrence nor increase adverse effects. As there was no statistically significant difference between the two treatments with respect to those outcomes, this should translate into equivalent quality of life scores, but data are not available.

Clinicians may choose to use this procedure for many reasons, including the following patient benefits: shorter times to hospital discharge, less pain, smaller incisions, and earlier return to work. Although time to return to work was not a measured outcome of interest in any of the RCTs reviewed, it has been measured in past trials (2) and was noted in two of the trials included in this review (6,8). Those possible patient benefits are offset by the longer operating times associated with laparoscopic surgery, which affects both the clinicians and the support teams performing the procedure and the resources in the institutions where the procedure is performed.

Before laparoscopic surgery can be considered one of the standards of practice for treatment with curative intent of colon cancer within the Province of Ontario, two issues must be addressed. The institutions capable of providing the necessary infrastructure to support clinicians and the physicians best able to perform laparoscopic surgery for colon cancer need to be defined. However, identifying the minimum number of procedures to achieve competency has not been the explicit subject of study. Nonetheless, there is evidence from the trials that prior physician experience is a must, but the exact number of prior procedures ranged from an unstated value ("multiple"; 6) to at least 20 operations, for either all operating room team members (9) or at least one operating team member (7) (Table 3). The actual threshold to achieve equivalent patient outcomes might be less than 20, but, due to the lack of definitive guidance, accepting the 20 previous operations as stated in two of the trials (for either one team member or all team members) is not unreasonable until more data are available.

During the external review by Ontario clinicians and Hospital Administrators many questions were raised concerning implementation issues, but addressing these are beyond the scope of this clinical practice guideline and these issues will be addressed in a future document. The regional cancer programs in Ontario in partnership with the provincial Surgical Oncology Program will develop implementation strategies and evaluation studies to address these issues. Additionally, an implementation strategy and evaluation study that will address the broader

relationship between volumes and outcomes will be led by the Surgical Oncology Program (SOP) of Cancer Care Ontario as part of its overall quality improvement agendas.

In summary, laparoscopic surgery for colon cancer is an acceptable option for curative treatment in a specific group of patients and poses no increase in risk for patients, while being associated with a benefit in the duration of hospital stay, less pain, smaller incisions, and an earlier return to work.

ONGOING TRIALS (NCI® clinical trials database searched August 4, 2004).

Open Trial
Phase III randomized study of conventional versus laparoscopic-assisted surgery for colorectal cancer. Protocols: MRC-CLASICC; ISRCTN74883561; NYCTRU-CLASICC; EU-98014 • This is a randomized, multicentre study. • Patients undergo laparoscopic surgery or conventional open surgery. • Approximately 1,200 patients will be accrued for this study within 5 years. • Medical Research Council Clinical Trials Unit sponsorship.

CONCLUSIONS

The members of the LCCSEP concluded that laparoscopic surgery is an acceptable option for the treatment of stage I, II, or III colon cancer. They also concluded that at least one member of the surgical team should have completed a number of laparoscopic colectomies to a level of accepted competence. All eligible institutions should be committed to this procedure and should provide appropriate equipment, operating room time, and human resources.

CONFLICT OF INTEREST

All members of the LCCSEP were polled for conflicts of interest, and none were reported.

ACKNOWLEDGEMENTS

This project was led by a working group of the LCCSEP comprised of Andy Smith, Bryan Rumble, Hartley Stern, Bernard Langer, Farrah Schwartz and Melissa Brouwers. Special thanks to Andy Smith and Bryan Rumble for taking the lead in drafting this systematic review with meta-analysis.

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Evidence-based Series #2-20-2: Section 3

Laparoscopic Surgery for Cancer of the Colon: Guideline Development and External Review - Methods and Results

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A Quality Initiative of Cancer Care Ontario's
Surgical Oncology Program and the Program in Evidence-based Care

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THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-based Care (PEBC) is an initiative of the Ontario provincial cancer system, Cancer Care Ontario (CCO) (1). The PEBC mandate is to improve the lives of Ontarians affected by cancer, through the development, dissemination, implementation, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer care.

The PEBC supports a network of disease-specific panels, called Disease Site Groups (DSGs) and Guideline Development Groups (GDGs), mandated to develop the PEBC products. These panels are comprised of clinicians, methodologists, and community representatives from across the province.

The PEBC is well known for producing evidence-based practice guideline reports, using the methods of the Practice Guidelines Development Cycle (1,2). The PEBC reports consist of a comprehensive systematic review of the clinical evidence on a specific cancer care topic, an interpretation of and consensus agreement on that evidence by our DSGs and GDGs, the resulting clinical recommendations, and an external review by Ontario clinicians in the province for whom the topic is relevant. The PEBC has a formal standardized process to ensure the currency of each clinical practice guideline report, through the routine periodic review and evaluation of the scientific literature and, where appropriate, the integration of that literature with the original clinical practice guideline information.

The Evidence-based Series: A New Look to the PEBC Practice Guidelines

Each Evidence-based Series is comprised of three sections.

- *Section 1: Clinical Practice Guideline*. This section contains the clinical recommendations derived from a systematic review of the clinical and scientific literature and its interpretation by the DSG or GDG involved and a formalized external review by Ontario practitioners.
- *Section 2: Systematic Review.* This section presents the comprehensive systematic review of the clinical and scientific research on the topic and the conclusions reached by the DSG or GDG.

- *Section 3: Guideline Development and External Review: Methods and Results.* This section summarizes the guideline development process and the results of the formal external review by Ontario practitioners of the draft version of the clinical practice guideline and systematic review.

DEVELOPMENT OF THIS EVIDENCE-BASED SERIES

Development and Internal Review

This evidence-based series was developed by Cancer Care Ontario's Laparoscopic Colon Cancer Surgical Expert Panel (LCCSEP), as a collaborative project of the Surgical Oncology Program (SOP) and the Program in Evidence-based Care (PEBC). The series is a convenient and up-to-date source of the best available evidence on laparoscopic surgery for colon cancer, developed through systematic review, evidence synthesis, and input from practitioners in Ontario. This series is the first collaboration between Cancer Care Ontario's Surgical Oncology Program and the PEBC.

Provincial Panel Consensus Process

Members of the LCCSEP agreed unanimously with the interpretation of the evidence. For patients with colon cancer within the well-defined target population, laparoscopic surgery should be considered a treatment option based on the findings of no statistically significant differences for overall survival, recurrence, and adverse effects when compared with open surgery.

The main topic of discussion within the membership involved determining the proposed minimum standards for clinicians. The minimum number of prior procedures recommended in the Hazelbroek et al (3) and COST trials (4) were thought to be poorly defined and the true threshold for equivalent patient outcomes might well be less than 20; therefore, stating any minimum as the absolute standard of practice was seen as potentially limiting capable surgeons. To impose such a limitation without providing some plan of action detailing training and accreditation procedures would be viewed as restricting practice.

Disease Site Group Consensus Process

The draft guideline (version date February 21, 2005) was reviewed and discussed by the Gastrointestinal Cancer DSG on February 25, 2005. All members were in agreement regarding the following interpretation of the evidence: based on the evidence currently available there is no statistically significant difference between laparoscopic surgery (LAP) and conventional open surgery (CON) when used for resection with curative intent in the treatment of Stages I,II, or III colon cancer, with respect to overall survival and recurrence. However, significant differences were detected between LAP and CON surgery for length of hospital stay (favouring LAP) and duration of surgery (favouring CON).

The Gastrointestinal Cancer DSG agreed with the draft recommendations and motioned that the document be sent out for practitioner feedback.

External Review by Ontario Clinicians

Following review and discussion of sections 1 and 2 of this evidence-based series, the LCCSEP circulated the clinical practice guideline and systematic review to clinicians in Ontario for review and feedback. Box 1 summarizes the draft clinical recommendations and supporting evidence developed by the panel.

BOX 1:
DRAFT RECOMMENDATIONS (approved for external review June 8, 2005)

Target population

Adult patients with stage I, II, or III colon cancer (not rectal cancer).

- Who do not have perforation, obstruction, fistula, or attachment to other structures (locally advanced disease).

Draft Clinical Recommendation

Based on the clinical evidence, a consensus of expert opinion, and the experience of members of the Laparoscopic Colon Cancer Surgery Expert Panel (LCCSEP), the following recommendation was drafted:

- Laparoscopic surgery is recommended as an acceptable option for the treatment of stage I, II, or III colon cancer and should be considered an alternative to conventional open surgery for colon cancer in specified patients.

Qualifying Statements

- The patient population to whom this guideline applies was the standard population studied in the randomized controlled trial reviewed.
- These recommendations do not apply to patients with colon cancer associated with perforation, obstruction, fistula, or attachment to other structures (locally advanced disease). The recommendations do not apply to patients with rectal cancer as evidence is unavailable for this population.
- Possible contraindications to performing a laparoscopic colon resection include general contraindications applicable to colon surgery in general, those applicable to other laparoscopic procedures in general, or those specific to a subgroup of patients. Previous colon resection, significant obesity, or another major medical illness represent relative contraindications and should only be approached by experienced laparoscopic colorectal surgeons.

Draft Professional Practice Recommendations

- The Laparoscopic Colon Cancer Surgery Expert Panel recommends that surgeons should have completed a number of laparoscopic colectomies to a level of accepted competence, as determined by their peers in a structured mentoring process. The best evidence available indicates that primary outcomes are not statistically different between laparoscopic and open surgery for colon cancer after at least one member of the team has performed 20 procedures. The recommendation is that either this number be adhered to or an equivalent process, including peer evaluation, be undertaken.
- Surgeons are strongly encouraged to self-audit their experiences. The use of audit tools such as that championed by the Canadian Association of General Surgeons (CAGS) is recommended.

Draft Institutional and Organizational Recommendations

The LCCSEP recommends that all eligible institutions should show a commitment to advanced laparoscopic surgery by providing appropriate equipment, operating room time, and human resources, including developing a team approach to maximize the experience and efficiency of all team members.

Methods

Practitioner feedback was obtained through a mailed survey of 319 clinicians (comprised of general surgeons, gastrointestinal surgeons, gastroenterologists, etc.) and 121 administrators (hospital CEO's, etc) in Ontario, Canada, for a total of 440 potential respondents. The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations above should be approved as a practice guideline. Written comments were invited. The practitioner feedback survey was

mailed out on June 8, 2005. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The LCCSEP and the Gastrointestinal Cancer DSG reviewed the results of the survey.

Results

This analysis includes the 196 surveys that were returned as of August 8, 2005 (43.9% response rate). Responses include returned completed surveys as well as phone, fax, and email responses. Of the practitioners who responded, 186 (40.8%) indicated that the report was relevant to their clinical practice, and they completed the survey. Not all respondents answered all questions, and the total number of responses is noted for each question. Of the respondents, approximately 70% were surgeons, 26% were administrators, and 4% were unknown (either surgeons or administrators). Key results of the practitioner feedback survey are summarized in Table 1.

Eighty percent or more of the respondents agreed or strongly agreed that there was a need for guidance on this topic and that the methodologies used to develop the document were appropriate. In addition, there was significant agreement or strong agreement (>80%) with the recommendations, their clarity, suitability, and applicability for the patients for whom they are intended. There were varied perceptions around issues regarding implementation (e.g., service reorganization, technical challenges, and/or resource issues). This feedback will be extremely important in informing the implementation strategy of these recommendations. Finally, over 70% of respondents agreed or strongly agreed the draft should be approved as a practice guideline and they indicated they would use the recommendations in their own practice.

Table 1. Practitioner responses to eight items on the practitioner feedback survey.

Item	N	Number (%)		
		Strongly agree or agree	**Neither agree nor disagree**	**Strongly disagree or disagree**
There is a need for guidelines on this topic	151	95	4	1
The literature search is relevant and complete	144	80	13	3
I agree with the methodology used to summarize the evidence	147	87	9	2
The trial results were interpreted according to my understanding of the data	147	89	6	2
The draft recommendations in this report are clear	148	93	3	2
I agree with the draft recommendations as stated	147	82	11	5
The draft recommendations are suitable for patients for whom they are intended	147	88	7	3
The draft recommendations are too rigid to apply to individual patients	149	11	17	70
When applied, the draft recommendations will produce more benefits than harms	148	63	29	6
The draft recommendations present options that would be acceptable to patients	144	81	11	3
To apply the draft recommendations requires reorganization of service/care in my setting	149	52	14	33
To apply the draft recommendations will be technically challenging	148	48	20	30

The draft recommendations are too expensive to apply	149	24	28	47
The draft recommendations in this guideline are achievable	147	77	12	9
The draft recommendations present a series of options that are likely to be supported by the majority of my colleagues	148	68	22	9
The draft recommendations reflect a more comprehensive series of options for improving patient outcomes than is current usual practice	148	64	23	11
When applied, the draft recommendations will result in better use of resources use than current usual practice	148	26	35	16
I would be comfortable if my patients received the care recommended in the draft recommendations	147	88	7	3
The draft recommendations should be approved as a practice guideline	147	74	16	8
		Very likely or likely	**Unsure**	**Not at all likely or unlikely**
If this report were to become a practice guideline, how likely would you be to make use of it in your own practice?	148	71	11	16
If this report were to become a practice guideline, how likely would you be to apply these recommendations to your patients?	148	76	14	8

Summary of Written Comments

The majority of written comments supported the summary of the evidence and recommendation. Issues raised in the written comments fell into four main categories

Recommendation for 20 supervised procedures: Concerns emerging from this recommendation include the lack of direct evidence on which this advice is based, questions regarding its interpretation (e.g., time frame to attain competency, generalizability of other LAP procedures to apply to this competency), and the feasibility of its implementation,

Recommendation for mentoring program: Some respondents expressed concern about the feasibility of implementing this recommendation including whether there were sufficient number of trainers, appropriate infrastructure and resource support to create a provincial training program, etc.

Other implementation issues: Issues raised relating to implementation centred around appropriate support to create the appropriate multidisciplinary clinical team, expanded OR time for surgeons, support from funding agencies for appropriate equipment, and greater clarity regarding what defines an institution committed to advanced LAP surgery.

Other issues: A few clinical issue emerged in the written comments including a query why rectal cancer was not included, a suggestion to reiterate the need for 12 regional nodes to be checked, and a suggestion to include as a recommendation the need for a medical oncology consult in the event of positive nodes.

Modifications/Actions

With respect to the question of whether or not 20 supervised LAP procedures is an appropriate number, the LCCSEP would like to restate that the best evidence available was obtained from RCTs where a minimum of 20 LAP resections for colon cancer was the standard. For this reason, the LCCSEP continues to support the recommendation that 20 procedures be adhered to or an equivalent process, including peer evaluation, be undertaken. The LCCSEP

acknowledges that 20 procedures may be more than enough experience for some surgeons, while not quite enough for others; therefore there are some limitations to simply requiring 20 supervised procedures. As an alternative to this, the implementation of a well thought-out peer credentialing process may prove integral to facilitating knowledge transfer from experienced surgeon to the surgeon trainee. However, detailing this peer credentialing process is beyond the scope of this guideline. The LCCSEP would only support a peer credentialing program that would serve all interested surgeons, including those in remote or smaller centre, in a timely manner. It is true that some skills may be transferable to LAP resection for colon cancer including some of those listed in the previous section, and for this reason a peer credentialing program may have some advantages over 20 supervised procedures in facilitating knowledge transfer.

With respect to the issues raised related to mentoring, the LCCSEP acknowledges that for any province-wide LAP resection for colon cancer program to be successful appropriate surgeons must be identified as potential candidates for mentoring their peers, and that these candidates should be chosen by their peers. The LCCSEP is in complete agreement with the respondents who stressed that one of the key components to any successful mentoring program will be the full support, financial and otherwise, from Cancer Care Ontario and the Ontario Ministry of Health and Long-term Care. It is imperative that any mentorship program chosen must be capable of facilitating the transfer of knowledge in as expedient a time as possible in order to support clinicians, patients, and ongoing CCO/MOH wait times initiatives.

With respect to the issues of implementation and time constraints the LCCSEP agrees that there needs to be buy-in from the other affected health professionals such as nursing, pathology, and anaesthesia. These other professionals will need to contribute more time per LAP procedure, especially during early attempts by surgeons where OR times will be longer. While time per procedure may be reduced over time as surgeons become more familiar with LAP techniques, the current evidence suggests LAP resections take longer than open resections, even in the hands of experienced (>20 procedures) surgeons. Purchasing the proper LAP kit is integral for institutions, and funding entities need to support all eligible institutions, even those in smaller or more remote locations. The LCCSEP supports all surgeons being allocated enough OR time, which will vary from surgeon to surgeon, and from practice centre to practice centre. Supporting eligible institutions as they support their surgeons in adding LAP skills must be made a priority by the MOHLTC, and this may mean current funding formulas may need to be re-examined.

With respect to the other issues forwarded in the written comments, the LCCSEP submits the following:

- Where we state “eligible institutions” must show a commitment to advanced LAP surgery, we did not define what would make an institution eligible as this may entail some formal accreditation process which is beyond the scope of this guideline.
- Rectal cancer patients were excluded from the recommendations as there was no RCT evidence available to support the use of LAP resection for colon cancer for these patients.
- LAP is not being recommended over open resection for colon cancer in this guideline; the LCCSEP acknowledges that open resection is the gold standard intervention for these patients, however, for certain patients defined by the target population of this guideline, LAP resection is an acceptable alternative to open resection.
- Involvement of pathology is as important in LAP resection as it is in open resection, and clinicians should continue to check at least 12 regional nodes. Patients with positive nodes may be candidates for adjuvant therapy, and this should be considered within the primary care team.
- The potential benefit of LAP resection allowing for faster initiation of adjuvant therapy may be found to be true, but currently there is no evidence to either support or refute this.

Report Approval Panel

The final Evidence-based Series report was reviewed and approved by the PEBC Report Approval Panel (RAP), which consists of two members including an oncologist, with expertise in clinical and methodological issues. The main comments obtained from the RAP concerned the sections that dealt with the physician and institutional standards. It was noted by one reviewer that completing these sections represents a change from previous PEBC reports. The PEBC acknowledges that although adding these sections does represent a change from past practice, it is in line with the PEBC's quality improvement goals.

The following minor comments were addressed:

- The survival data for the Lacy trial in Table 1 incorrectly presented mortality numbers not survival numbers, and this was corrected in both the table and meta-analysis figure. This change did not affect outcome or interpretation.
- The meta-analyses figures do indeed reflect time-dependent outcomes, and the time periods for when the data were reported are now noted in the text.
- In the pooling of the adverse event rates no grading scale was used, these numbers represent the total number of adverse events reported. While there are methodological issues with combining data in this manner if the purpose was to draw some conclusion regarding a specific adverse effect, it is useful in calculating any difference observed between treatment and control rates wholly.
- It is now noted in the text that the pooled secondary outcomes (operating times and time until hospital discharge) were unweighted as standard deviations were not reported in the studies.
- The ages of CON patients now appear with the ages of LAP patients in Table 4.
- References supporting LAP patients returning to work earlier have been added to the text where appropriate.
- A section on Quality of the Evidence Reviewed has now been added to the systematic review portion of this clinical practice guideline.

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