Laparoscopic Surgery for Cancer What are the issues?

R Sim

Centre for Advanced

Laparoscopic Surgery, TTSH

National Healthcare Group

Adding years of healthy life

CALS

The Issues

- Feasibility and safety
- Adequacy - same radical surgery as open op.
- Efficacy – short term benefits and long term oncologic results
- Time and Cost – is it worth the effort?
- Training and certification – who can be accredited?

Basic science considerations

- Laparoscopic environment
- CO2 pneumoperitoneum
- Port-site metastases
- Immune function

Intraperitoneal exfoliated cancer cells in patients with colorectal cancer. Hase et al. DCR Sep 1998

Positive pre-cytology 15%, post-cytology9%

Post-cytology stronger influence on LR than pre-cytology; LR rate in positive post-cytology higher than those with negative post-cytology, regardless of pre-cytology.

All with positive post-cytology had recurrence.

Features of tumor prone to exfoliate (1)macroscopic dissemination (2)liver mets (3)>20ml ascites (4)ulcerated without definite borders (5)invade beyond serosa (6) semiannular or annular (7)lymphatic invasion

Prognostic value of microscopic peritoneal dissemination – comparison between colon and gastric cancer. Vogel et al. DCR Jan 2000;43(1):92-100.

Colon cancer - Conventional cytology positive 35.5%

Immunocytology positive 47.2%

Gastric cancer - Conventional cytology positive 42.3%

Immunocytology positive 46.8%

Associated with pTNM staging

Microscopic peritoneal dissemination influences survival time after R0 resections only in gastric but not colon cancer.

The influence of a pneumoperitoneum on the peritoneal implantation of free intraperitoneal colon cancer cells. Hubens et al. Surg Endosc 1996; 10:809-12.

I - midline laparotomy, IP injection

II – IP injection alone

III – pneumo after IP injection

IV – trocars inserted after pneumo and IP injection

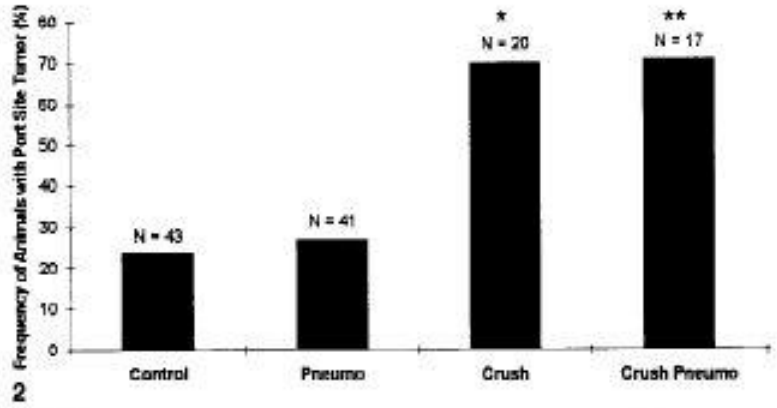
Similar implantation rates of 50-60%

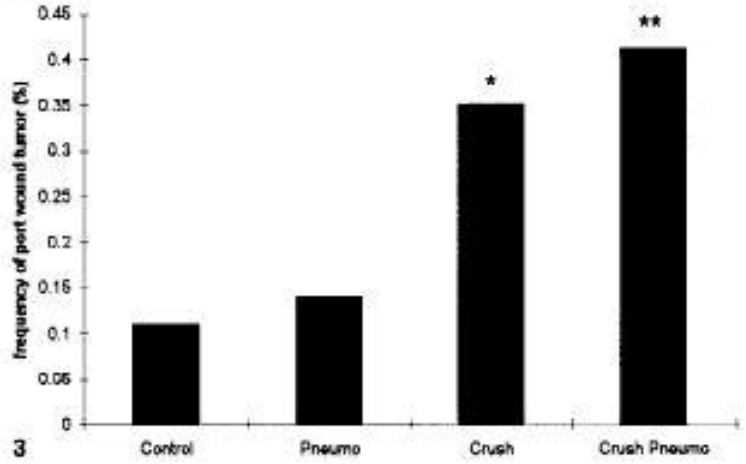
Pneumoperitoneum does not enhance implantation of free intraperitoneal malignant colon cancer cells in the rat.

CO_2 pneumoperitoneum does not enhance tumor growth and metastases - Study of a rat cecal wall inoculation model. Tomita et al. DCR Sep 2001; 44(9):1297-1301.

	CO_2 pneumo	Laparotomy
Cecal tumor growth	1.043g	0.894g
Liver mets	32%	37%
Lung mets	34%	17%
Lymph node mets	84%	77%
Wound/port mets	20%	23%

Traumatic handling of the tumor independent of pneumoperitoneum increases port site implantation rate of colon cancer in a murine model. Lee et al. Surg Endosc 1998;12:828-34.





Surgical technique plays a larger role in the development of port site tumors than CO2 pneumoperitoneum

Fig. 2. Comparison of frequency of animals with port site tumor implantation by intervention. $*p <$ 0.001, control versus crush. $**p <$ 0.002, pneumo versus crush pneumo.

Fig. 3. Comparison of trocar site tumor incidence by intervention. $*p < 0.001$, control versus crush. $**p < 0.001$, pneumo versus crush pneumo.

Does Laparoscopic *vs.* Conventional Surgery Increase Exfoliated Cancer Cells in the Peritoneal Cavity During Resection of Colorectal Cancer? Kim et al. DCR Aug 1998;41(8):971-8.

- After the abdominal cavity was entered, saline was instilled into the peritoneal cavity, and the fluid was collected (Specimen 1). During surgery, all irrigating fluids were collected (Specimen 2). Both were assessed for malignancy using four techniques: filtration process (ThinPrep), smear, cell block, and immunochemistry using Ber-EP4.
- Malignant cells were not detected in any Specimens 1 or, more importantly, in Specimens 2 in either surgical group.

Increased tumor establishment and growth after open vs laparoscopic bowel resection in mice. Allendorf et al. Surg Endosc 1998;12:1035-8.

	Tumor established	Tumor mass
Control	5%	75±68 mg
Laparoscopic	30%	115±68 mg
Open	83%	180±132 mg

Port site metastases and recurrence after laparoscopic colectomy – A randomised trial.

Lacy et al. Surg Endosc 1998;12:1039-42.

End-points - mets at port-sites and laparotomy incisions

- recurrence rate

No wounds or port-site mets in both open and laparoscopic

RR 16.1% for LAC, 15% for OC

Effect of port composition on tumor cell adherence: an in vivo model. Brundell et al. DCR May 2003;46(5):637-42.

Reduce number of tumor cells deposited in port-sites

- Minimise number of tumor cells in peritoneal cavity
- Plastic ports rather than metal ports
- Secure ports to prevent displacement

Beneficial in reducing port-site mets

Efficacy of surgical measures in preventing port-site recurrences in a porcine model.

Schneider et al. Surg Endosc 2001;15:121-5.

Trocar fixation	
Prevent gas leak	
Povidone iodine rinse	Port-site implantation
- instruments, trocars and wound	13.8%(5/36) vs 63.8% (23/36)
Wound protection	
Peritoneal closure	

ORIGINAL CONTRIBUTION

Short-term Quality-of-Life Outcomes Following Laparoscopic-Assisted Colectomy vs Open Colectomy for Colon Cancer

A Randomized Trial

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Context Laparoscopic-assisted colectomy (LAC) has emerged as the preferred minimally invasive surgical strategy for diseases of the colon. The safety and efficacy of LAC for colon cancer are unknown, and the nature and magnitude of any quality-of-life (QOL) benefit resulting from LAC for colon cancer is also unknown.

Objective To compare short-term QOL outcomes after LAC vs open colectomy for colon cancer.

Design, Setting, and Participants Multicenter, randomized controlled trial (Clinical Outcomes of Surgical Therapy [COST]). Between September 1994 and February 1999, 37 of 48 centers provided data for the QOL component of the trial for 449 consecutive patients with clinically resectable colon cancer.

Main Outcome Measures Scores on the Symptoms Distress Scale (SDS), Quality of Life Index, and a single-item global rating scale at 2 days, 2 weeks, and 2 months postoperative; duration of postoperative in-hospital analgesic use; and length of stay.

Results Of 449 patients, 428 provided QOL data. In an intention-to-treat analysis comparing SDS pain intensity, SDS summary, QOL Index summary, and global rating scale scores at each time point, the only statistically significant difference observed between groups was the global rating scale score for 2 weeks postsurgery. The mean (median) global rating scale scores for 2 weeks postsurgery were 76.9 (80) for LAC vs 74.4 (75) for open colectomy ($P=.009$). While in the hospital, patients assigned to LAC required fewer days of both parenteral analgesics compared with patients assigned to open colectomy (mean [median], 3.2 [3] vs 4.0 [4] days; $P<.001$) and oral analgesics (mean [median], 1.9 [1] vs 2.2 [2] days; $P=.03$).

Conclusion Only minimal short-term QOL benefits were found with LAC for colon cancer compared with standard open colectomy. Until ongoing trials establish that LAC is as effective as open colectomy in preventing recurrence and death from colon cancer, this procedure should not be offered to patients with colon cancer.

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ALTHOUGH LAPAROSCOPIC TECHniques were first described in 1901,[1] only in the past few years have newer optics and instrumentation allowed for the safe application of laparoscopic resection procedures. The first report of a successful laparoscopic cholecystectomy in 1987 was followed by rapid widespread adoption of the procedure.[2-6] In recent years, laparoscopic procedures for a number of other nonmalignant abdominal diseases, including appendicitis, inguinal hernia, gastroesophageal reflux disease, hiatal hernia, and nonmalignant uterine conditions, have become routine. The interest in laparoscopic approaches for these conditions has been driven by the theoretical benefits, including reduced postoperative pain, shortened length of stay, and earlier return to work, and perhaps by the technological imperative.[5,6]

Improvements in both technology and surgeons' comfort and skill with laparoscopic techniques have led to an interest in extending the indications for laparoscopic surgery to include curative resection of colon cancer. In laparoscopic-assisted colectomy (LAC), mobilization of the bowel is conducted laparoscopically and then the bowel is externalized for resection and anastomosis. Laparoscopic-assisted colectomy has emerged as the preferred minimally invasive strategy for colonic

See also p 377 and Patient Page.

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Conclusion Only minimal short-term QOL benefits were found with LAC for colon cancer compared with standard open colectomy. Until ongoing trials establish that LAC is as effective as open colectomy in preventing recurrence and death from colon cancer, this procedure should not be offered to patients with colon cancer.

Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial

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Summary

Background Although early reports on laparoscopy-assisted colectomy (LAC) in patients with colon cancer suggested that it reduces perioperative morbidity, its influence on long-term results is unknown. Our study aimed to compare efficacy of LAC and open colectomy (OC) for treatment of non-metastatic colon cancer in terms of tumour recurrence and survival.

Methods From November, 1993, to July, 1998, all patients with adenocarcinoma of the colon were assessed for entry in this randomised trial. Adjuvant therapy and postoperative follow-up were the same in both groups. The main endpoint was cancer-related survival. Data were analysed according to the intention-to-treat principle.

Findings 219 patients took part in the study (111 LAC group, 108 OC group). Patients in the LAC group recovered faster than those in the OC group, with shorter peristalsis-detection (p=0·001) and oral-intake times (p=0·001), and shorter hospital stays (p=0·005). Morbidity was lower in the LAC group (p=0·001), although LAC did not influence perioperative mortality. Probability of cancer-related survival was higher in the LAC group (p=0·02). The Cox model showed that LAC was independently associated with reduced risk of tumour relapse (hazard ratio 0·39, 95% CI 0·19–0·82), death from any cause (0·48, 0·23–1·01), and death from a cancer-related cause (0·38, 0·16–0·91) compared with OC. This superiority of LAC was due to differences in patients with stage III tumours (p=0·04, p=0·02, and p=0·006, respectively).

Interpretation LAC is more effective than OC for treatment of colon cancer in terms of morbidity, hospital stay, tumour recurrence, and cancer-related survival.

Lancet 2002; **359:** 2224–29

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Introduction

Colorectal cancer is the second leading cause of cancer-related death in Western countries. Prognosis associated with this disease has improved due to early diagnosis and changes in medical therapy. Adjuvant chemotherapy in colon cancer, radiotherapy, and introduction of the total mesorectal excision technique in rectal cancer have increased survival, especially in patients with stage III tumours. Moreover, oxaliplatin and irinotecan have improved the prognosis associated with metastatic colorectal cancer.[1]

Laparoscopic surgery has led to great progress in the treatment of many gastrointestinal diseases.[2] Early reports on laparoscopy-assisted colectomy (LAC) in patients with colon cancer suggest that it lowers surgical trauma, decreases perioperative complications, and leads to more rapid recovery.[3–6] However, development of port-site metastases in some cases showed that this approach was questionable.[7,8]

Few preliminary data that compare LAC with open colectomy (OC) in colon cancer have been reported. They suggest that LAC is associated with reduced perioperative morbidity and very low risk of wound metastasis.[4,6,9,10] However, there are no studies that compare LAC and OC in terms of tumour recurrence and survival.

In this article we report the results of a randomised trial in patients with non-metastatic colon cancer. The aim of the trial was to assess whether there are differences in cancer-related survival between LAC and OC.

Methods

Patients

From November, 1993, to July, 1998, all patients admitted to our unit with adenocarcinoma of the colon, 15 cm above the anal verge, were assessed. Exclusion criteria were: cancer located at the transverse colon, distant metastasis, adjacent organ invasion, intestinal obstruction, past colonic surgery, and no consent to participate in the study.

Randomisation was done the day before surgery. Patients were stratified in two groups according to tumour location (right or left side, with respect to the splenic flexure), and subsequently assigned to LAC or OC by means of sealed opaque envelopes containing computer-generated random numbers. To prevent selection bias, random numbers were generated by an investigator (AC) who was not involved in enrolment of participants.

Due to the limited evidence about LAC at the beginning of the study, interim analyses that assessed early morbidity, tumour recurrence, and port-site metastasis were planned during the first period.[9,10] The study was approved by the institutional ethics of research committee and oral consent was obtained from each patient.

Interpretation LAC is more effective than OC for treatment of colon cancer in terms of morbidity, hospital stay, tumour recurrence, and cancer-related survival.

This superiority of LAC was due to differences in patients with stage III tumours

Conclusion

We have to work harder
so that patients heal better