

Laparoscopic-Assisted Resection of Colorectal Malignancies

A Systematic Review

Andrew E. Chapman, BA (Hons),* Michael D. Levitt, FRACS,† Peter Hewett, FRACS,‡ Rodney Woods, FRACS,§ Harry Sheiner, FRACS,|| and Guy J. Maddern, FRACS, PhD¶

From the *Australian Safety & Efficacy Register of New Interventional Procedures–Surgical (ASERNIP-S) project, Royal Australasian College of Surgeons, Adelaide, South Australia; †Sir Charles Gairdner Hospital, Perth, Western Australia; ‡Department of Surgery, Queen Elizabeth Hospital, Woodville, South Australia; §Departments of Colorectal Surgery, St. Vincent's and Box Hill Hospitals, Melbourne, Victoria, Australia; ||Western Australian Clinical Oncology Group, Western Australia; and ¶Queen Elizabeth Hospital, Adelaide, South Australia

Objective

To compare the safety and efficacy of laparoscopic-assisted resection of colorectal malignancies with open colectomy.

Methods

Two search strategies were devised to retrieve literature from the Medline, Current Contents, Embase, and Cochrane Library databases until July 1999. Inclusion of papers was determined using a predetermined protocol, independent assessments by two reviewers, and a final consensus decision. English language papers were selected. Acceptable study designs included randomized controlled trials, controlled clinical trials, case series, or case reports. Fifty-two papers met the inclusion criteria. They were tabulated and critically appraised in terms of methodology and design, outcomes, and the possible influence of bias, confounding, and chance.

Results

Little high-level evidence was available. Laparoscopic resection of colorectal malignancy was more expensive and time-consuming, but little evidence suggests high rates of port site recurrence. The new procedure's advantages revolve around early recovery from surgery and reduced pain.

Conclusions

The evidence base for laparoscopic-assisted resection of colorectal malignancies is inadequate to determine the procedure's safety and efficacy. Because of inadequate evidence detailing circumferential marginal clearance of tumors and the necessity of determining a precise incidence of cardiac and other major complications, along with wound and port site recurrence, it is recommended that a controlled clinical trial, ideally with random allocation to an intervention and control group, be conducted. Long-term survival rates need to be a primary aim of such a trial.

Since the introduction of laparoscopic cholecystectomy, laparoscopic techniques have been applied to a variety of benign colorectal conditions, including inflammatory bowel disease and diverticular disease.¹ These successes have prompted the development of laparoscopic techniques for the resection of adenocarcinoma of the colon and rectum.^{2,3} Techniques range from full laparoscopic procedures, incor-

porating both intracorporeal resection and anastomosis, to laparoscopic-assisted procedures where a portion of the procedure is done extracorporeally.

Theoretical benefits of laparoscopic colectomies have been extracted from experience with laparoscopic cholecystectomy: faster recovery of pulmonary function; less pain from smaller incisions; decreased narcotic use, leading to faster return of intestinal motility; a lower rate of wound complications; and more rapid mobilization of patients, leading to a shortened hospital stay and quicker return to normal activities⁴—to which has been added lower costs⁵ and improved cosmesis.^{6,7} Owing to the increased complexity of laparoscopic colectomy compared with laparoscopic cholecystectomy, the exact extent of the purported benefits

The Australian Commonwealth Department of Health and Aged Care supported the Australian Safety & Efficacy Register of New Interventional Procedures–Surgical (ASERNIP-S) project.

Correspondence: Guy J. Maddern, FRACS, PhD, ASERNIP-S, P.O. Box 688, North Adelaide, 5006, Australia.

E-mail: college.asernip@surgeons.org

Accepted for publication January 17, 2001.

is not yet clear.⁵ Also, it is unclear whether such techniques can achieve adequate oncologic resection and staging.⁵ Of great concern is the apparently high rate of tumor recurrence at laparoscopic port sites.⁸

It is the purpose of this review to assess the safety and efficacy of laparoscopic or laparoscopic-assisted procedures for the resection of colorectal malignancies (LARCM) compared with traditional open surgical procedures.

In 1995, colorectal cancers were the most common type of cancer in Australia (after prostate cancer). They were the second most common cancer causing death in women and the third most common cancer causing death in men.⁹ Adenocarcinomas of the colon and rectum are often curable if the tumor has not metastasized to lymph nodes or other organs. The primary treatment is surgery with the intent to cure.¹⁰ Surgery is usually performed through a long midline abdominal incision with ligation of vessels, resection of the primary tumor with adequate margins of at least 5 cm distally and proximally, complete local lymphadenectomy, and the construction of a safe anastomosis.^{4,10,11} An additional aim in open colorectal surgery is to stage the malignancy through palpation of the liver or through pathologic examination of resected lymph nodes and the tumor specimen itself. Accurate staging of colorectal malignancy has important implications for survival rates, as well as for the decision to apply adjuvant therapies.²

Rates of complications and death for standard colorectal cancer surgery have been reported to range from 8% to 15% and 1% to 2%, respectively. The most serious complications include anastomotic leakage, obstruction, and infection. Surgery for rectal cancer is associated with additional serious complications such as disruption of the autonomic nerves, which can result in urinary retention and loss of sexual function, as well as incontinence and locoregional recurrence after sphincter-preserving procedures.¹¹ Exposure of the colon through a long abdominal incision and mechanical retraction allows the surgeon to perform extensive procedures in the abdominal cavity, although the price for this excellent exposure is postoperative pain, tissue trauma, intraoperative and postoperative metabolic stress, and postoperative ileus.⁴

Laparoscopic or laparoscopic-assisted colorectal procedures vary according to which portion of the bowel is being resected but typically involve four abdominal incisions or ports through which the camera and instruments are inserted via cannulas and the specimen is retracted. If the resected specimen is removed through a small (usually muscle-splitting or Pfannenstiel-type incision) minilaparotomy, the anastomosis may be performed extracorporeally.

The decision to use entirely laparoscopic versus laparoscopic-assisted techniques is largely dependent on the location of the pathology.¹² Complete laparoscopic procedures involve an intracorporeal resection and anastomosis and are typically performed for left-sided lesions.¹³ Although it is possible to perform a completely laparoscopic procedure for left-sided lesions, some authors have expressed reservations

Table 1. POSSIBLE MECHANISMS THAT LEAD TO PORT SITE METASTASIS

Mechanical
Direct contamination
Seeding during extraction of tumor through a small wound
Seeding by contact with instruments contaminated with tumor cells
Indirect contamination
Seeding into the wound during episodes of desufflation of the pneumoperitoneum
Cells exist in an aerosol and are transferred to wounds and ports without direct contamination (chimney effect).
Metabolic/immunologic
Seeding occurs in both open and laparoscopic wounds, but metastases are more likely after laparoscopy because of locally acting immunologic and/or metabolic factors.
Hematogenous
Seeding by hematogenous spread during surgery

Adapted from reference 65.

about the wisdom of this in the treatment of malignant disease owing to the possibility of tumor seeding during transanal retrieval of the resected specimen, along with the danger of mechanical damage to the sphincter.^{4,14-17} Others maintain that transanal retrieval should avoid some of the factors involved in extraction-site implantation, although they admit that large specimens may present problems.¹⁸ Whatever the site of extraction, it is increasingly acceptable to retrieve the specimen in an impermeable bag to prevent tumor spillage.⁴

Many authors have noted the existence of a steep learning curve for laparoscopic colectomies, a fact that has probably skewed complication and death rate data from the series reported for this procedure, many of which are drawn from initial experiences with LARCM.⁴ Others have suggested that it is only in the palliation of abdominal cancer that the laparoscopic technique may have its best application.¹⁹

Port site metastases are early tumor recurrences occurring in the abdominal wall within the scar tissue of one or more trocar sites after laparoscopy for cancer. Various causes have been postulated to explain these recurrences, including the use of the CO₂ pneumoperitoneum,¹⁴ contamination of the trocars with cells exfoliated from the primary tumor that implant in the abdominal wall when the devices are extracted,²⁰⁻²³ and as sequelae of complications of surgical drainage.²⁴ Possible mechanisms are summarized in Table 1.

Initially, the incidence of port site recurrences was reported to range between 1.5% and an alarming 21%, although a broader analysis suggested a rate closer to 4%.⁸ These sorts of figures led some critics to argue that LARCM should be confined to randomized trials or ceased altogether until the mechanisms responsible for these recurrences are understood and appropriate countermeasures developed.²⁵ However, wound recurrences are also not unknown after conventional open procedures, with a much-quoted rate of 0.8% for a series of 1,603 patients treated with curative

resection between 1950 and 1980,²⁶ and a more recent estimate of 0.64% based on 1,711 curative resections performed from 1986 to 1989.²⁷ These rates are in line with a more recent examination of the published laparoscopic data that suggests a more reassuring figure for wound and port site implantation of 0.85% across 1,769 cases.²⁸ This suggests that the earlier, apparently high incidence of port site tumors may have been a result of early surgical experience and technical problems. There may be wide inconsistencies in surgical technique between surgeons or in the techniques that the individual surgeons apply when performing laparoscopic or open procedures,^{17,29} which has led some to conclude that the single most relevant factor involved in port site implantation in a clinical setting is surgical technique, not such factors as pneumoperitoneum.³⁰

METHODS

Review Process

A surgeon familiar with the topic of review (protocol surgeon) and an Australian Safety & Efficacy Register of New Interventional Procedures—Surgical (ASERNIP-S) researcher worked together to draft the protocol for the systematic review and determined the studies to be included. The ASERNIP-S researcher assessed these publications and produced a systematic review, which was critiqued by a surgeon who is familiar with the topic under investigation but who does not typically perform the procedure (advisory surgeon). The protocol, review, and critique formed the review documentation, which was considered by the review group. The review group comprised the advisory and protocol surgeons, a nominated surgeon from the Colon & Rectal Section of the Royal Australasian College of Surgeons, a surgeon from another specialty, and an ASERNIP-S researcher. The review group considered the review documentation, recommendations, and ASERNIP-S classifications put forward by the ASERNIP-S researcher and advisory surgeon. Once consensus was reached on the recommendations and classifications, they were presented to the ASERNIP-S management committee and subsequently to the Royal Australasian College of Surgeons Council for ratification.

Search Strategy

Original published studies on LARCM were identified by searching Medline between 1984 and July 1999, Current Contents between 1993 and July 1999, Embase between 1974 and July 1999, and the Cochrane Library between 1984 and 1999 (issue 2). The search terms used were as follows: (colectomy or colectom* or hemicolectom* or resection) and (laparoscop* or endoscop* or minimal* invasive) and (colorectal or rect* or colon* or intestine, large) and (neoplasm* or adenoma* or malignanc* or cancer* or adenocarcinoma* or carcinoma* or tumor* or tumor* or

Table 2. OUTCOME CRITERIA FOR STUDY INCLUSION

1. 3-year and 5-year disease-free survival rates
2. Postoperative deaths
3. Postoperative complications
4. Oncologic factors
5. Postoperative pain—number of days of narcotic analgesia, pain score
6. Duration of surgery
7. Start of oral food intake
8. Length of hospital stay
9. Total hospital costs
10. Time to resumption of normal activities
11. Conversion rate
12. Immunologic response

metastas* or neoplastic) not (FAP or familial adenomatous polyposis or HNPCC or hereditary nonpolyposis or inflammatory bowel disease or ulcerative colitis or Crohn* or diverticulitis). A different, broad strategy for the Cochrane Library database was used because the restricted search turned up too few references. The simple search term used was “colectomy.” The truncation symbol “*” differs in each database and allows retrieval of all suffix variations of a root word.

Only full, peer-reviewed articles were included because abstracts did not provide adequate detail on patient selection, allocation, study design, outcome, and measurement methods to allow an accurate, unbiased assessment and comparison of the study results.

Inclusion Criteria

Papers were selected for inclusion if they were in English and were randomized controlled trials (RCTs), controlled clinical trials, case series, or case reports. Only human studies were included, specifically if all the participants had adenocarcinoma of the colon. Studies needed to relate to LARCM, including right, sigmoid, or left hemicolectomy with or without colostomy. Controlled clinical trials were selected if the comparative intervention included similar colorectal resection via laparotomy. However, for technical as well as cancer reasons, papers were excluded if they confounded outcomes for either the new or comparative intervention with abdominoperineal resections, transverse colectomies, or total colectomies. Papers were included if they provided information on at least one outcome, as defined in Table 2.

Data Extraction

The protocol surgeon and ASERNIP-S researcher assessed articles for suitability using the inclusion criteria. Unsuitable and duplicate studies were deleted from the literature database.

Table 3. DESIGNATION OF LEVELS OF EVIDENCE

1	Evidence obtained from a systematic review of all relevant randomized controlled trials
2	Evidence obtained from at least one properly designed randomized controlled trial
3-1	Evidence obtained from well-designed pseudorandomized controlled trials (alternate allocation or some other method)
3-2	Evidence obtained from comparative studies with concurrent controls and allocation not randomized (cohort studies), case-control studies, or interrupted time series with control group
3-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group
4	Evidence obtained from case series, either posttest or pretest/posttest

Data from reference 66.

Data Analysis

All relevant studies were assessed as to their level of evidence (Table 3). The studies were tabulated and methodologically evaluated, including appropriateness of exclusion criteria, quality of reporting, and possible confounding variables. All data and results of statistical tests were extracted from the papers. In the case of concurrently controlled studies, measures of effect (relative risk, relative risk reduction, and odds ratios) were calculated. Measures of effect were not calculated for historically controlled studies because the bias and confounding inherent in that study design meant that the risk measures were uninterpretable. No meta-analyses were performed.

For particular outcomes of interest, papers were included in the analysis only if they specifically reported on the item of interest and no assumptions were made from the presence of missing data. For example, with complication rates, papers that did not report a complication rate were not assumed to have reported a zero rate of complications but were treated as if the data were missing and were thus excluded from complication analyses.

RESULTS

After exclusions, the literature search retrieved 52 studies. Most had various methodologic or reporting deficiencies, which (excluding case reports) are summarized in Table 4.

A possible source of confounding to which many studies fell prey was the inclusion of patients with both potentially curable and incurable cancers. This, of course, has profound implications on any analysis of survival rates but may also affect the type and frequency of complications reported, and other perioperative details such as surgical times and costs. Some studies presented good matching by tumor grade of

patients in experimental and control groups,^{31,32} but in most it was potentially a source of considerable variance.

There were frequent problems in extracting useful data from many studies because the authors frequently amalgamated data for procedures both excluded and included by the review protocol. Hence, for many papers only a portion of the overall data could be meaningfully retrieved and used in the subsequent analyses. Another related concern is when authors conglomerated or compared data from different procedures included in the protocol, but which might have been more meaningfully dealt with separately (e.g., anterior resections with right hemicolectomies). Where the data could be reported separately, this has been done; where they could not, appropriate caveats have been drawn in the analysis.

No studies used masking for surgical procedures, although this is not remarkable considering the blatant differences between laparoscopic and open colectomies. Several studies did, however, use masked pathologists or others to assess surgical specimens, whether to perform lymph node counts or to measure margin lengths and gross specimen dimensions.³³⁻³⁷ However, at least one critic has pointed out that the use of laparoscopic vascular staplers would give the pathologist a clue as to which technique was used to recover the specimen.³⁸ No studies explicitly addressed this issue.

The level 2 studies were generally of good quality, although two^{31,33} excluded patients from the LARCM group if the laparoscopic procedure was converted to an open procedure, thus introducing a selection bias and obviating the advantages of randomization. This violates the intent-to-treat rule, a cardinal principle of clinical research, and a shortcoming, among others, for which the latter of these two studies has been criticized elsewhere.³⁸ Principally, though, the level 2 studies suffered from small sample sizes, with the largest study recruiting 71 patients³⁹ and the smallest only 16.³¹

At least four of the level 3-2 studies also violated the intent-to-treat rule by excluding converted subjects. However, three of these papers appeared to report on the same study.^{34,40,41} Because there were novel data elements in each of these three papers, they are treated separately here where applicable. A strength of four of these studies (counting the three prior as one) was the comparison of single types of colectomies rather than comparing mixtures of procedures (e.g., right hemicolectomies with anterior resections). Three papers, however, included invalid procedures for the study protocol, thus severely limiting the utility of the data for this review (see Table 4).

The level 3-3 and level 4 papers were largely of poor quality, with 20 of 22 papers including invalid procedures or not reporting study details in sufficient detail to assess the validity of the procedures, thus presenting restricted data sets (see Table 4). In addition, most of these papers failed to summarize the study populations or procedures in satisfactory detail or, owing to the exclusion of subjects because of

Table 4. METHODOLOGIC SUMMARY OF ALL HUMAN NONCASE REPORTS BY LEVEL OF EVIDENCE

Study	Local/Metastatic	Violates Intent to Treat	Reports Single Procedure Only*	Includes Invalid Procedures	Poor Reporting of Study Details
2					
Hewitt ³¹	L	Yes			
Kim ⁴³	L & M				
Lacy ^{39,42}	L & M				
Stage ³³	L & M	Yes			
3-2					
Bokey ³⁴	L & M	?	Yes		
Buchmann ⁵³	L & M				
Franklin ³⁵	L & M			Yes	
Fukushima ⁵⁷	L	Yes	Yes		
Goh ⁵¹	L & M		Yes		
Khalili ³⁶	L & M	Yes		Yes	
Leung ⁴⁴	L & M				
Lord ⁵⁹	L & M			Yes	Yes
Moore ⁴¹	L & M	Yes	Yes		
Phillipson ⁴⁰	L & M	Yes	Yes		
Tate ⁵²	L & M		Yes		
3-3					
Gellman ⁶⁷	?			Yes	Yes
Leung ³²	L & M				
Musser ⁶⁸	?			Yes	Yes
Van Ye ⁶⁰	?			Yes	
4					
Baca ⁶⁹	L & M	Yes		Yes	Yes
Bokey ³⁷	L & M			Yes	Yes
Cohen ⁷⁰	L			Yes	
Cook ²³	Mainly M			Yes	Yes
Dean ⁷¹	?			Yes	Yes
Delgado ⁵⁴	L & M			Yes	
Delgado ⁴⁸	L & M			Yes	
Guillou ⁷²	?			Yes	Yes
Hoffman ⁴⁵	L & M†				Yes
Jacobs ⁷³	?			Yes	Yes
Konishi ⁵⁸	?			Yes	Yes
Leung ⁵⁵	L & M			Yes	
Molenaar ⁴⁶	L & M‡			Yes	
Quattlebaum ⁴⁷	?			Yes	Yes
Ramos ⁴⁹	?			?	Yes
Vara-Thorbeck ⁵⁶	M			Yes	
Vukasin ⁵⁰	?			?	Yes
Zucker ⁷⁴	?			Yes	Yes

L, Dukes A, B or C, or specific exclusion of metastatic disease; M, Dukes D or metastatic disease.

* Only one type of colectomy reported on (e.g., only left hemicolectomies rather than left and right).

† Excluded metastatic from death rate data.

‡ Changed exclusion criteria during study from L & M to M.

invalid procedures, these details could not be derived for the restricted class of subjects remaining after these exclusions were made.

Safety

The safety of a medical intervention can be assessed as the level of risk inherent in the procedure to cause injury or harm to its recipients. Because most if not all surgical procedures carry measurable risks, the question of safety

can be framed in terms of which of two or more alternative procedures is the least likely to cause harm to the patient. The risks associated with surgical procedures are also likely to be multifactorial; hence, a surgical procedure may be riskier than a comparator when some measures are applied but safer when other yardsticks are used. Three broad measures of safety have been used in this review: complications, cancer recurrence rates, and death and survival rates. Clearly, death and survival rates are the central issue for any surgical intervention for cancer.

Table 5. PERIOPERATIVE DEATH RATES

Study	Level of Evidence	Death Rate		Relative Risk Reduction
		Laparoscopic	Open	
Hewitt ³¹	2	0% (n = 8)	0% (n = 8)	...
Lacy ³⁹	2	0% (n = 31)	0% (n = 40)	...
Bokey ³⁴	3-2	4% (n = 28)	0% (n = 33)	...
Leung ⁴⁴	3-2	4% (n = 28)	4% (n = 56)	0%
Leung ³²	3-3	2% (n = 50)	6% (n = 50)	...
Bokey ³⁷	4	5% (n = 55)
Delgado ⁵⁴	4	0% (n = 31)
Guillou ⁷²	4	7% (n = 45)
Leung ⁵⁵	4	1% (n = 140)
Vara-Thorbeck ⁵⁶	4	0% (n = 17)
Zucker ⁷⁴	4	0% (n = 31)

Death Rates

Comparative data for perioperative deaths were generally poor, even though most of the reporting studies were RCTs. One reported a 0% death rate for both the LARCM and open groups, but only over a 21-day follow-up period and with only 16 subjects.³¹ Two of the other RCTs were apparently earlier and later reports of the same study, or at least appeared to share some of the same subjects; for this reason, the earlier⁴² has been disregarded here in favor of the later.³⁹ It, too, reported a 0% death rate in both groups. One RCT failed to report any death rate data at all.⁴³ The last RCT failed to report whether the three deaths occurring among its subjects occurred in the LARCM or open procedure groups, and—although noting that these three had liver metastases at the time of surgery—failed to note the ultimate cause of death.³³

Only two non-RCTs reported perioperative death rate data;^{34,44} neither found significant differences between the two groups and both had wide confidence intervals for relative risk (3.52, 95% confidence interval [CI] 0.15–83.08; and 1.00, 95% CI 0.09–10.56). Another study compared death rates in a LARCM group with those of historical controls, reporting a rate of 2% in the former and 6% in the latter.³² Data for case series are summarized along with those for the comparative studies in Table 5. Perioperative death rates varied widely, with figures ranging from 0% to 7%.

Long-Term Survival Rates

Again, the quality of data was poor. Only one RCT reported long-term survival data, finding a nonsignificant increase in relative risk of 1.61 (95% CI 0.47–51) for death in the LARCM group versus the open group with a follow-up of at least 12 months (mean 21.4 ± 11.5).³⁹ All deaths were cancer-related. The initial cancer profile of the two groups was not identical, though, with five stage D1 cancers in the LARCM group and only two in the open group. Similarly, the LARCM deaths tended to occur in

patients with more advanced cancers. In the LARCM group, four deaths occurred in patients with stage D1 cancers and one occurred in a patient with a C2 cancer. In the open group, two patients with B2, one with a C2, and one with a D1 carcinoma died. The power of this study was extremely low (estimated at 0.06).

The one non-RCT with contemporaneous controls that provided any data was also the only paper to have a 5-year follow-up.⁴⁴ It found that the LARCM group had a nonsignificant survival odds ratio of 1.63 versus open controls, with 90.9% of LARCM patients surviving 5 years (compared with only 55.6% of patients undergoing the traditional open procedure). Open control subjects were matched to laparoscopic patients by age, gender, tumor stage, and tumor size, so the quality of this study appears high, even though subjects were not randomized. Exclusion criteria for the LARCM group were explicitly stated, but those for the open group were described only as being similar, so some selection bias may have entered the study here, along with the usual risks associated with nonrandomized studies.

The only other paper containing comparative data for long-term follow-up used historical controls³² and found little difference in survival rates, with 67.2% of LARCM patients surviving 4 years compared with 64.1% of open controls. Five case series addressed to various degrees long-term survival in patients undergoing LARCM. Results are summarized in Table 6. The 20% survival rate for LARCM reported by one case series of five patients is unremarkable when one considers that the follow-up period was defined as being until patient death.²³

Recurrence

There were few comprehensive cancer recurrence data in the literature. Disregarding port site recurrence, only one RCT,³⁹ one non-RCT,⁴⁴ one non-RCT with historical controls,³² and three case series^{45–47} reported recurrence rates for carcinoma, with rates between 4% and 16%. All recurrence rates were reported for between 20 months and 3

Table 6. LONG-TERM SURVIVAL RATES FOR LAPAROSCOPIC COLECTOMIES

Study	Level of Evidence	Time Period	Survival Rate		Odds Ratio*
			Laparoscopic	Open	
Lacy ³⁹	2	21.4 ± 11.5 months	84% (n = 31)	90% (n = 40)	0.93
Leung ⁴⁴	3-2	21.4 months (median)	90.9% (n = 28)	55.6% (n = 56)	1.63
Leung ³²	3-3	32.8 months (median)	67.2% (n = 50)	64.1% (n = 50)	...
Cook ²³	4	Until patient death	20% (n = 5)
Delgado ⁴⁸	4	42 months	AR: 83%; S: 87% (n = 31)
Hoffman ⁴⁵	4	2 years	Node-negative: 92%; (n = 39) Node-positive: 80%
Molenaar ⁴⁶	4	3 years	All: 59%; by stage: (n = 35) A = 86%, B = 66%, C = 68%, D = 0%
Quattlebaum ⁴⁷	4	Approx. 8 months	90% (n = 10)

AR, anterior resection; S, sigmoid resection.

* Odds ratio is used rather than relative risk because survival is a desirable outcome; it is calculated in a similar manner to relative risk.

years, except for one case series that reported a recurrence rate of 10% after approximately 8 months. Relative risk reduction for the LARCM groups in the RCT and non-RCT were calculated at -8% and 78%, respectively, when compared with open patients. However, none of the comparative studies found a significant difference in recurrence rates between the LARCM and open groups.

Similarly, the data for disease-free survival rates were poor. No RCTs reported on this information, and only two non-RCTs^{32,44} (one of which used historical controls) and two case series^{45,48} reported any results, and all for differing time periods, ranging from 2 to 5 years (Table 7). Neither of the comparative studies showed markedly inferior disease-free outcomes for the LARCM groups versus the open groups; rather, both presented nominally superior outcomes for LARCM, although neither result was significant.

Presumably because of the interest generated by early reports of port site recurrence, the reporting of results for this type of recurrence was much more comprehensive. Four

of the five RCTs^{33,39,42,43} reported specifically on port site recurrences, although none found any recurrence. Overall, including the case series but excluding the case reports, 14 instances of port site recurrence were reported out of 1,114 cases, although more than half of these cases were drawn from two surveys of the same registry of laparoscopic bowel procedures.^{49,50} To avoid double-counting, only the later of these two is included in the analysis here. This survey may have included subjects who had undergone laparoscopic colorectal procedures that were excluded by the protocol for this review. The paper gave insufficient detail as to patient selection and treatment but is included here because of the large subject base it provides for this important issue. Some confidence can be gained from the high response rate of 97.4%, although the submission of cases to the registry appears to have been voluntary; thus, there is the possibility of selection bias. However, after excluding the one survey, there were 11 instances of port site implantation reported out of 862 cases, giving a rate of 1.28% (95% CI 0.64–2.27). No instances of wound recurrence were reported for the open colectomy subjects in any of the comparative studies that returned data on this topic.

Complications

Overall Studies using concurrent controls showed a broad range of differences in overall complication rates between LARCM groups and open groups, with relative risk reductions for LARCM ranging from 75%⁵¹ to -59%.⁵² For several of these studies,^{35,36,53} overall complication rates could not be calculated because of the inclusion in the study population of patients undergoing procedures excluded by this report's protocol or because of the use of historical controls.³² Of the RCTs that reported complication rates, only one paper³¹ reported no complications for both groups. The sample size for this paper was small (n = 16), and patient selection may have favored patients who were otherwise in good condition, because patients

Table 7. DISEASE-FREE SURVIVAL RATES

Study	Time Period	Survival Rate		Odds Ratio*
		Laparoscopic	Open	
Leung ⁴⁴	5 years	95.2%	74.7%	1.27
Leung ³²	4 years	80.5%	72.9%	...
Delgado ⁴⁸	42 months	AR: 78% S: 70%
Hoffman ⁴⁵	2 years	Node-negative: 96% Node-positive: 79%

AR, anterior resection; S, sigmoid resection. Node status refers to presence of metastases in lymph nodes at time resection was performed.

* Odds ratio is used rather than relative risk because survival is a desirable outcome; it is calculated in a similar manner to relative risk.

older than 80 years or those with advanced cancers or other debilitating diseases were excluded. More critically, this study also violated the intent-to-treat principle, excluding one subject who was converted from laparoscopic to open colectomy. Of the remaining two papers, one⁴² reported a significant reduction in risk of 61% for LARCM, whereas risk reduction could not be calculated for the other³³ (reporting only two complications overall, both in the laparoscopic group). However, as previously stated, this latter study also had a selection bias favoring LARCM, because converted subjects were excluded.

The other nonrandomized concurrently controlled studies for which complication data were available present an inconclusive picture. Only one of the papers presented a positive relative risk reduction (75%);⁵¹ the other three showed relative increases in risk of 8% to 59% for LARCM when compared with the open procedure.^{34,44,52} However, the paper that reported a risk reduction for LARCM selected patients for the open procedure by the presence of a palpable abdominal mass and selected patients for LARCM by the absence of such a mass, a selection bias that would seem to favor the LARCM group. In addition, there were slightly more advanced cancers (stage D) and slightly fewer early cancers (stage A) in the open group. Also, the paper that reported the least increase in relative risk³⁴ excluded six (18%) LARCM patients who were converted to an open procedure. Reasons for conversion included accidental port injury to the cecum (n = 1), tumor adherence to the duodenum (n = 1), dense adhesions (n = 1), development of hypercapnia (n = 1), and lack of progress (n = 2). Further complications were not reported for this subgroup, thus threatening to invalidate the complication data from this paper.

To increase the statistical power of its results, one of the remaining two papers matched each LARCM patient with two open patients using sex, age, tumor stage, tumor length, tumor site, and extent of resection (all randomly selected from a larger pool of patients who underwent open resection in the same period) for a total pool of 84 patients.⁴⁴ It found a relative increase in risk of 33% for the LARCM group.

Relative risks and confidence intervals for the three studies that had no obvious selection biases are suggestive of equivalent complication outcomes for both the laparoscopic and open procedures.^{42,44,52} However, caution should be applied in combining the results of RCTs and non-RCTs because the non-RCTs are more likely to be prone to unknown selection biases and confounding variables.

Including case series, a total of 11 papers produced overall complication data for LARCM, with a wide range of 0% to 75%.^{31-34,42,44,51,52,54-56} Because these figures cannot be meaningfully conglomerated, it is problematic to calculate an overall complication rate for LARCM.

The wide variability in reported complication rates presents an intractable problem. One can only speculate on the source of this variation: it might reflect varying sensitivities of different authors to what constitutes a reportable compli-

Table 8. ALL REPORTED COMPLICATIONS FOR LAPAROSCOPIC COLECTOMIES

Complication	n	%
Wound infections	30	5.7
Respiratory	16	3.1
Cardiac	15	2.9
Hemorrhage	10	1.9
Anastomotic leaks	8	1.5
Urinary tract infections	3	0.6
Small bowel perforations	3	0.6
Port site herniation	2	0.4
Hematoma	2	0.4
Septicemia	1	0.2
Peritonitis	1	0.2
Anastomotic stricture	1	0.2
Anastomotic edema	1	0.2
Hypoxia	1	0.2
Acute renal failure	1	0.2
Discompensated renal insufficiency	1	0.2
Urinary retention	1	0.2
Deep vein thrombosis	1	0.2
Small bowel obstruction	1	0.2
Phlebitis	1	0.2
Intraabdominal abscess	1	0.2

Case reports were excluded.

ation, or it might reflect a broad variability in surgical technique or experience. Other possible reasons include differing protocols for patient selection, different study designs, or even the fact that different procedures under the colectomy banner might be prone to greater or lesser complication rates.

Specific Complications Across all papers, including case series, for which overall complication data could be calculated, the most common types of complications related to LARCM were wound infections, respiratory complications, and cardiac complications. A diverse range of other complications were reported in small numbers (Table 8). Several port site recurrences and instances of peritoneal carcinomatosis were also noted and are discussed below. Ileus was commonly reported as overall mean (or median) time to flatus or first bowel sound rather than defining and counting specific instances. Occasionally mean (or median) time to first bowel movement was reported. There were no RCTs that found significant differences in specific complications rates between LARCM and the traditional open procedure. Only one RCT⁴² found any significant difference related to complications, and that was with the duration of ileus. Patients undergoing LARCM were found to have a shorter duration (35.5 ± 15.7 hours) than patients treated in the conventional manner (71.1 ± 33.6). None of the three non-RCTs^{34,52,57} that reported results on the duration of ileus found any significant difference between LARCM and the open procedures.

No RCTs or non-RCTs found any significant difference

Table 9. RELATIVE RISKS FOR SELECTED COMPLICATIONS: LAPAROSCOPIC VERSUS OPEN

Study	Wound Infections	Cardiac Complications	Respiratory Complications
Lacy ⁴²	0.52 (0.10–2.59)	3.12 (0.13–73.07)	Not estimable
Leung ⁴⁴	9.83 (0.49–198.05)	5.90 (0.25–140.28)	1.00 (0.09–10.56)
Tate ⁵²	6.25 (0.33–118.22)	Not estimable	0.42 (0.02–9.34)

95% confidence intervals are given in parentheses.

in the amount of blood loss between the LARCM and open groups,^{33,42,51,57} nor in the number of blood transfusions received by patients.³³ The quality of data for blood loss and transfusions was poor across these studies, with one⁴² using means and standard deviations when medians and ranges would have been more appropriate (because of highly skewed data) and others either not adequately reporting figures^{35,53} or not reporting them at all, yet still making assertions with regard to statistical significance.⁵⁷

With regard to the three most common complications reported in comparative studies (wound infection, respiratory complications, and cardiac complications) and drawing on the same group of papers considered above to be most free of obvious bias, it was not possible to conclude that LARCM is associated with either an increased or decreased risk of complication when compared with the open procedure (Table 9). All of the 95% CIs of the relative risk estimates encompass unity, and most are extremely broad.

Efficacy

The efficacy of a procedure, although naturally related to safety issues, is principally concerned with how effectively

the surgical intervention achieves the technical goals that are not directly related to issues of safety. In this section the question is whether LARCM produces equivalent technical outcomes to the standard open procedure. However, the last of the indicators examined here is closely related to safety and deals with oncologic factors such as the comprehensiveness of the resection and lymph node recovery; however, because most of these oncologic indices are of a technical nature, they are included in the efficacy section. The other indicators relate to the duration of surgery, the speed of postoperative recovery, and conversion rates.

Duration of Surgery

One of the most consistent findings across the comparative studies examined here is that LARCM takes longer than the traditional open procedures. Of the three RCTs that measured this variable,^{31,33,42} all found significant differences in surgical times. After excluding one non-RCT that duplicated the results of another,³⁴ there were five non-RCTs^{40,44,51,52,57} with contemporaneous controls and one non-RCT with historical controls³² that compared the duration of surgery. Three of the five found significant differences between LARCM and the open procedure; the other two were both close to significance ($P = .08$).

As can be seen in Table 10, the difference in the duration of surgery between the two procedures is not only highly significant but is also nontrivial, with most studies showing a mean or median difference of around an hour or more. No paper gives any indication that LARCM is faster than the traditional open procedure.

Conversion Rates

Conversion rates of LARCM to open colectomy varied widely, from 0% to 46% (Table 11). The highest rates were reported in papers that clearly stated that the series resulted from early experience,^{46,48} although early experience was not necessarily associated with high conversion rates.⁵⁶ For

Table 10. MEAN OR MEDIAN DURATION OF OPERATION

Study	Level of Evidence	n	Mean or Median Duration (min)			P Value
			Laparoscopic	Open	Difference	
Hewitt ³¹	2	16	165 (130–300)*	107.5 (90–150)*	57.5	.02
Lacy ⁴²	2	51	148.8 (±45.5)†	110.6 (±49.3)†	38.2	.006
Stage ³³	2	29	150 (60–275)*	95 (40–195)*	55	.05
Fukushima ⁵⁷	3-2	14	231 (±23)‡	169 (±20)‡	62	.08
Goh ⁵¹	3-2	40	90 (55–185)*	73 (40–140)*	17	.08
Leung ⁴⁴	3-2	84	191.8 (±34.5)†	148.6 (±41.7)†	43	<.001
Philipson ⁴⁰	3-2	61	261.0 (±13.7)†	203.0 (±9.1)†	58	<.001
Tate ⁵²	3-2	25	205 (±31)†	123 (±26)†	82	.01
Leung ³²	3-3	100	196.1 (±44.4)†	149.5 (±61.1)†	46.6	<.001

* Data are given as median (range).

† Data are given as mean (± standard deviation).

‡ Standard error.

Table 11. CONVERSION RATES BY SURGEON EXPERIENCE IN PERFORMING LAPAROSCOPIC COLECTOMIES

Study	Level of Evidence	n	Conversion Rate	Documented Surgeon Experience
Hewitt ³¹	2	8	11%	Significant
Lacy ⁴²	2	25	16%	Wide exp. with laparoscopic techniques
Stage ³³	2	15	17%	All senior surgeons trained in lap & open
Bokey ³⁴	3-2	28	18%	Among first 127 patients
Franklin ³⁵	3-2	160	4%	Probably some early experience
Goh ⁵¹	3-2	20	0%	?
Leung ⁴⁴	3-2	28	14%	Exp. in both lap and colorectal procedures
Leung ³²	3-3	50	16%	Median 9 (8–19) years
Bokey ³⁷	4	55	15%	Probably early experience
Delgado ⁴⁸	4	31	AR 46%; S 28%	First 50 cases
Guillou ⁷²	4	45	11%	Series extended from early experience
Molenaar ⁴⁶	4	35	26%	Early experience
Vara-Thorbeck ⁵⁶	4	17	0%	Possibly early experience

AR, anterior resection; S, sigmoid resection.

most studies surgeon experience was not clearly stated. For a substantial proportion of other papers, conversion rates could not be calculated because of conglomeration of such data between procedures excluded and included in the review's protocol.

Postoperative Recovery

Most studies that attempted to assess the severity of postoperative pain did so by measuring analgesic use in terms of number of doses or amount given. A single RCT³¹ found a significant difference in morphine requirements between the LARCM and open groups, with subjects treated with the experimental procedure requiring less pain relief (median 27 mg morphine vs. 62 mg in the first 48 hours; $P = .04$). Patients mainly underwent sigmoid and anterior resections and controlled their own morphine administration, either via intravenous morphine infusion or intramuscular bolus injection of pethidine on demand. The failure of this study to respect the intent-to-treat principle has been discussed earlier.

Of the two non-RCTs with contemporaneous controls that measured pain relief requirements in terms of number of doses, one⁴⁴ reported no significant difference in analgesia use between the two groups and the other⁵² found that the LARCM group used significantly less analgesia. Possible explanations for the differences between these two studies may include different procedures being performed across groups or different analgesic regimens being followed.

Two other non-RCTs with contemporaneous controls attempted to assess analgesic need by measuring the number of days during which analgesia was required by patients.^{34,51} Neither found any significant difference between the two groups. Number of days of analgesic use is not the same measure as number of doses (because the number of

doses may be spread over variable time periods), so a direct comparison with the previously mentioned studies is not valid. The first study consisted entirely of patients undergoing anterior resection. It specified that parenteral morphine was patient-controlled, but that the length of postoperative analgesia was determined by an anesthetist's assessment, which suggests that the study may actually have been measuring how long anesthetists think analgesia should be administered rather than validly assessing patient pain. The second study, in which patients underwent right hemicolectomies, did not specify the analgesic regimen other than to indicate that it was parenteral. It also violated the intent-to-treat principle.

Another RCT³³ measured levels of fatigue and pain using a visual analog scale, which was not described in the paper but was referenced. This paper suffered in quality by not reporting precise figures and also by excluding subjects from the LARCM group if they were converted to an open procedure, thus violating the intent-to-treat principle. However, the authors asserted that the patients undergoing LARCM reported significantly less pain when at rest 6 hours after surgery and overall compared with patients in the open group. Patients who underwent LARCM also achieved significantly lower pain scores on mobilization and coughing at 6 hours, although not at later periods. There was no difference between the groups in terms of fatigue.

The evidence appears to suggest that patients undergoing LARCM have either an equal or reduced level of pain compared with patients undergoing the traditional open procedure. Patients undergoing low colonic procedures such as anterior or sigmoid resections may benefit most. There is no evidence that LARCM results in an increased pain burden.

The single RCT that examined time until resumption of a solid diet found that patients undergoing LARCM began

Table 12. DURATION OF HOSPITAL STAY

Study	Level of Evidence	n	Mean or Median Duration of Hospital Stay (days)			P Value
			Laparoscopic	Open	Difference	
Hewitt ³¹	2	16	6 (5–7)*	7 (4–9)*	1	Not calculated
Lacy ⁴²	2	51	5.2 (±1.2)†	8.1 (±3.8)†	2.9	.0006
Stage ³³	2	29	5 (3–12)*	8 (5–30)*	3	.01
Bokey ³⁴	3-2	61	12 (±?)†	12.2 (±?)†	0.2	NS
Fukushima ⁵⁷	3-2	14	17 (±1.4)†	23.3 (±2.2)†	5.3	<.05
Goh ⁵¹	3-2	40	5 (3–10)*	5.5 (4–29)*	0.5	.13
Leung ⁴⁴	3-2	84	5 (2–12)*	7 (4–53)*	2	.002
Lord ⁵⁹	3-2	96	AR 5.3 (±?)† RH 5.8 (±?)†	AR 8.6 (±?)† RH 7.3 (±?)†	3.3 1.5	<.05 NS
Tate ⁵²	3-2	25	12.3 (±3)†	14.3 (±6)†	2	.79
Leung ³²	3-3	100	6 (3–22)*	8 (3–28)*	2	<.001

AR, anterior resection; RH, right hemicolectomy; NS, nonsignificant (*P* not specified).

* Data are given as median (range).

† Data are given as mean (± standard deviation).

food intake significantly sooner than patients in the open group.⁴² The difference in mean time to resumption was almost by a factor of two, with the LARCM patients resuming solids 50.9 hours on average after surgery compared with 98.8 hours for open patients.

The evidence from the four non-RCTs with contemporaneous controls is less clear-cut. One of the studies found that patients undergoing LARCM were significantly quicker to return to a normal diet than the open group.⁴⁴ Similarly, another reported that LARCM patients were significantly faster to resume solids than the open group.⁵² However, the other two non-RCTs^{34,51} reported no significant differences in time to resumption of solids between the two groups. The single non-RCT that compared return to solid diet in LARCM patients with historical controls also found no significant difference.³² The two non-RCTs that also measured time to start of oral fluids^{34,51} found no significant difference between the LARCM and open groups, as well as no difference in time to resumption of solid diet.

Three RCTs compared length of hospital stay between LARCM and open colectomy groups. One did not report on whether a statistical test of significance was performed, but the sample size was small ($n = 16$) and the medians and ranges similar (6 [5–7] vs. 7 [4–9]).³¹ The other two RCTs both reported that patients undergoing LARCM were significantly more likely to be discharged earlier from the hospital than those undergoing the open procedure.^{33,42} However, as discussed previously, the second of these studies introduced selection bias into the LARCM group by excluding from analysis those patients who were converted to an open procedure; thus, presumably only the less complicated laparoscopic cases were counted, and these patients might be expected to be discharged earlier anyway.

Results from the six non-RCTs with contemporaneous controls were mixed (Table 12). Three studies found no significant difference between patients undergoing LARCM

and open resections in the duration of hospital stay. Two found that hospital stay was significantly shorter in the patients undergoing LARCM (although one of these⁵⁷ was also obviously flawed by violating the intent-to-treat principle). One paper reported that the duration of hospital stay was significantly shorter for patients undergoing laparoscopic anterior resection but that there was no difference between patients undergoing laparoscopic or open right hemicolectomies. The single non-RCT that used historical controls found a significant reduction in hospital stay for LARCM patients.

Although these results seem diverse and somewhat contradictory, and the evidence base is not of particularly high quality, it is possible to see from the grouped data that no single study reported a mean or median hospital stay for patients undergoing LARCM that was either equal to or greater than the mean or median hospital stay of the particular comparative open group. This suggests (if not definitively) that the purported benefits of a reduced hospital stay for patients undergoing LARCM may be substantive.

Other measures of postoperative recovery were attempted by only a few studies. One RCT calculated a self-care score for its subjects from such items as fluid intake, bowel and bladder function, washing, mobility, and mental needs.³³ It found that patients undergoing LARCM scored significantly higher than open controls, suggesting a quicker return to normal self-care. The shortcomings in patient selection of this study have been discussed previously, however, and the results, isolated as they are, should be treated with more than the usual caution.

Another non-RCT compared return to full ambulation between laparoscopic and open right hemicolectomy patients, reporting that LARCM patients returned to full ambulation significantly sooner (2.7 vs. 3.4 days).³⁴ However, this paper also suffered from the same selection bias as the previous RCT that could be expected to favor the laparo-

Table 13. NUMBER OF LYMPH NODES RESECTED IN ALL COMPARATIVE STUDIES

Study	Level of Evidence	Lymph Nodes (Mean or Median)		Statistics
		Laparoscopic	Open	
Lacy ⁴²	2	13 (± 5.4)† (n = 25)	12.5 (± 7.7)† (n = 26)	NS
Stage ³³	2	7 (3–14)* (n = 15)	8 (4–15)* (n = 14)	NS
Buchmann ⁵³	3-2	14.3 ($\pm ?$)† (n = 41)	10.6 ($\pm ?$)† (n = 41)	...
Franklin ³⁵	3-2	15.9 ($\pm ?$)† (n = 160)	12.5 ($\pm ?$)† (n = 174)	...
Goh ⁵¹	3-2	20 (7–49)* (n = 20)	19 (7–97)* (n = 20)	NS (P = .44)
Khalili ³⁶	3-2	10 (± 1)† (n = 26)	11 (± 2)† (n = 25)	NS (P = .45)
Leung ⁴⁴	3-2	16 (5–29)* (n = 28)	16 (4–81)* (n = 56)	NS (P = .84)
Lord ⁵⁹	3-2	AR 7.8 ($\pm ?$);† (n = 47) RH 11.6 ($\pm ?$)†	AR 8.9 ($\pm ?$);† (n = 49) RH 10.1 ($\pm ?$)†	NS; NS
Moore ⁴¹	3-2	16.9 (± 1.9)† (n = 32)	15.9 (± 1.1)† (n = 34)	NS (P = .65)
Tate ⁵²	3-2	10 (2–14)* (n = 11)	13 (2–18)* (n = 14)	...
Gellmann ⁶⁷	3-3	9.5 ($\pm ?$)† (n = 56)	9.3 ($\pm ?$)† (n = ?)	...
Leung ³²	3-3	9 (2–28)* (n = 50)	8 (3–25)* (n = 50)	NS (P = .44)
Musser ⁶⁸	3-3	RH 12.2 ($\pm ?$); (n = 9– 14) LH 8.5 ($\pm ?$)†	?	...
Van Ye ⁶⁰	3-3	10 (± 8.1)† (n = 12)	? (n = 16)	...

AR, anterior resection; NS, not significant; RH, right hemicolectomy.

* Data are given as median (range).

† Data are given as mean (\pm standard deviation).

scopic group. A series of case reports found that each of three patients returned to full ambulation only 1 day after LARCM.⁵⁸

Oncologic factors

Of great concern is whether LARCM provides an equivalent radicality of resection compared with that of the open procedure. Requirements of an adequate cancer operation include suitable margins, adequate lymph node dissection, and containment of tumor and prevention of spillage of cancer cells into either the peritoneal cavity or adjacent lumen of the bowel. The first two of these indices have been most commonly measured by direct pathologic examination (pinning and measuring of specimens and lymph node dissection) and the last is sometimes approached via the mechanism of peritoneal lavage and counting of tumor cells. A related issue is patient immune response.

Of the 31 papers that reported summary statistics for the adequacy of lymph node dissection, there were 9 that compared outcomes of LARCM with the traditional open procedure. These were two RCTs,^{33,42} six non-RCTs with contemporaneous controls,^{34,36,41,44,51,59} and one non-RCT with historical controls.³² Two of the non-RCTs reported on the same study^{34,41} (to avoid double-counting, the former paper is excluded from further discussion in this section), and the selective shortcomings of one of the RCTs have been mentioned previously.³³ None found any significant difference between the procedures in terms of the number of lymph nodes recovered. In only one of these papers was the difference in the mean or median number of lymph nodes recovered in either procedure greater than one.⁵⁹

The reverse was true, however, in the six studies that did not attempt (or did not report) statistical analysis of the two procedures. Three reported differences of at least three in the mean or median number of lymph nodes recovered; two^{35,53} suggested a superior outcome for LARCM and the other the reverse.⁵² Reporting of data in five of six of these papers was inadequate, with means but no standard deviations published (the other reported median lymph nodes recovered), and two reporting no data for the comparator at all (Table 13). None of these six studies was an RCT. In summary, it seems safe to suggest, tentatively, that LARCM produces as adequate a lymph node recovery as the traditional open procedure.

With regard to tumor margins, the evidence is less clear. Of the 12 studies that reported results for length of resected tumor margins, there were 6 that provided statistical comparisons between patients undergoing LARCM and open procedures. Only one of these was an RCT³³ (and that flawed by excluding conversions), three were non-RCTs with contemporaneous controls,^{41,51,59} and one was a non-RCT with historical controls.³² Only two of these papers produced significant results when resected tumor margins were compared between the LARCM and open groups; both were non-RCTs with contemporaneous controls (Table 14). One reported superior recovery of distal margins during laparoscopic-assisted anterior resection, but similar margin recovery for right hemicolectomy.⁵⁹ The other reported superior recovery of distal margins during open right hemicolectomy.⁴¹ This same paper was the only study to compare separately proximal margin recovery, finding no significant differences between the two procedures.

Table 14. MARGINS RESECTED

Study	Level of Evidence	Resection	Distal Margins (cm)		Statistics
			Laparoscopic	Open	
Stage ³³	2	Mixed (right, left, & sigmoid)	4 (3–12)*‡	4 (3–12)*‡	NS
Goh ⁵¹	3-2	Anterior resection	4 (2–8)*	4.5 (3–7.5)*	NS (<i>P</i> = .35)
Lord ⁵⁹	3-2	Right hemi.	3.5 (±?)†	6.1 (±?)†	NS
		Anterior resection	4.9 (±?)†	2.5 (±?)†	SD (<i>P</i> < .05)
Moore ⁴¹	3-2	Right hemi.	10.0 (±1.2)†	13.9 (±1.1)†	SD (<i>P</i> = .006)
			10.1 (±1.3)†§	12.0 (±1.8)†§	NS (<i>P</i> = .44)
Leung ³²	3-3	Mixed (sigmoid & anterior resection)	3.0 (0.5–8.0)*	3.5 (1.0–11.0)*	NS (<i>P</i> = .36)

NS, not significant; SD, significant difference.

* Data are given as median (range).

† Data are given as mean (± standard deviation).

‡ Proximal/distal not specified.

§ Proximal.

Another method that some papers used to measure the adequacy of resection was the length of bowel resected. Three non-RCTs^{35,52,53} and two case series^{54,56} reported on this measure, although none attempted any analysis and the quality of reporting among the non-RCTs was generally poor, with two of the three papers providing no measure of variance. The third paper, which measured resected bowel lengths for anterior resections alone, produced similar figures for both the open (median 15 cm) and LARCM (median 14 cm) groups. In all, these attempts to measure resected bowel length seem to have produced little that is informative.

Another important issue is whether LARCM liberates larger numbers of cancer cells into either the lumen of the bowel or the peritoneal cavity compared with the open procedure. This has been proposed as a possible mechanism to explain the incidence of port site recurrence subsequent to LARCM. Only one paper attempted to measure whether this purported phenomenon occurs.⁴³ An RCT of good quality, this paper found no evidence for exfoliated cancer cells in the pre- or postresection peritoneal lavage of either the LARCM or the open groups.

Surgical Stress and Immune Response

Three papers addressed the issue of surgical stress and immunologic response to laparoscopic surgery. All measured levels of interleukin-6 (IL-6), a cytokine that, according to the authors of one of the studies, is known to modulate immunosuppression after surgery and appears to be a major mediator of the acute-phase response in humans, with increases in level reflecting the degree of surgical trauma.³¹

Of the two RCTs, one found no significant difference in IL-6 levels between patients undergoing LARCM and open procedures,³¹ whereas the other found significantly increased IL-6 levels in the LARCM group.³³ The first of these papers appears to be of a superior design, because patients who had received immune-modulating drugs,

blood, or blood products (factors known to affect immune response) in the previous 6 months were excluded, and narcotic use (also known to affect immune response) was standardized. This type of careful selection and treatment of subjects appears to have been overlooked in the second study. However, both papers suffered in quality for other reasons that have been discussed earlier. The first paper also had too few subjects (*n* = 16). Hence, the evidence from the RCTs appears to be inconclusive.

The single non-RCT with contemporaneous controls also found that on the day of surgery, IL-6 levels were significantly increased in the LARCM group compared with open controls.⁵⁷ This study also found that IL-6 levels were significantly and positively correlated with the duration of the procedure (*r* = 0.582), which was (not significantly) longer in the LARCM group (although see the section on surgical factors above). Although correlations do not imply causation, this result raises the plausible suggestion that any of the purported trauma-reducing benefits of the minimally invasive LARCM approach might be obviated by the stresses induced by the increased complexity and duration of this procedure. Unfortunately, this was also the lone study to address the issue in this manner. In addition, this study was based on a small sample of 14 nonrandomized patients and suffered from the same failure to respect intent to treat as the two RCTs.

Other stress-sensitive analyses were also performed in these studies. C-reactive protein levels were assessed by one of the two RCTs³³ and the non-RCT discussed above. The former reported a significant increase in levels in the LARCM group and the latter found no significant difference between the LARCM and open groups, as well as finding no differences in levels of plasma glucagon and urinary epinephrine. The other RCT also measured and found no significant differences between groups in levels of lymphocytes, monocytes, granulocytes, lymphocyte subfractions, and human leukocyte antigen expression on monocytes.

The limited evidence on the human immune system effects of laparoscopic versus open colectomy for adenocarcinoma appear to suggest that the situation is possibly more complex than originally proposed, with no evidence of superiority for the laparoscopic approach and, indeed, some small suggestion that the complexity of the procedure may result in greater surgical stress, at least in the short term. However, the clinical significance of these results remains unclear, and, as discussed below, these results contradict the broader literature on the immune and stress effects of laparoscopic surgery.

Costs

Only two papers compared the hospital costs associated with LARCM and open colectomies. Both were non-RCTs with contemporaneous controls. These papers reported on the same study, so the less detailed³⁴ has been excluded from further discussion in this section, leaving only one comparative cost study.⁴⁰ This study found that in terms of total hospital costs from the day of surgery to the day of discharge, broken down into direct and indirect hospital costs, staff costs, and cost of disposables, the LARCM group incurred significantly higher costs than the open colectomy group (overall mean costs of A\$9,064 vs. A\$7,881). The only cost measure on which the two were not significantly different was pharmacy, which was also the least expensive cost grouping overall. Unfortunately, this study excluded LARCM patients who were converted to open procedures. Because conversion could be expected to incur additional expenses, it seems plausible that the figures given here are particularly conservative, and, as discussed earlier, conversion also appears to be a relatively common phenomenon in LARCM (see Table 11). Additional shortcomings of this study were as follows:

- It was retrospective.
- It made no attempt to assess postdischarge costs incurred by patients.
- By directly comparing costs of two surgical procedures without making any measure of effectiveness, the study has the unwritten assumption that LARCM and open colectomies are equivalent and can be meaningfully compared in terms of direct costs. It made no attempt to conduct a cost-benefit or cost-effectiveness analysis.
- The study represents the early experience of surgeons with LARCM, but not necessarily early experience with open procedures. This is potentially a serious source of error.

An American non-RCT with historical controls also reported cost data.⁶⁰ Unfortunately, this study had poor reporting of control data, and because its subject pool contained many patients who were excluded from consideration by this review's protocol, it was not possible to disentangle cost data for the relevant portion of the control subjects. Hence, no comparison was possible, and only the LARCM

group's data could be reported. The mean cost for this patient group was US\$19,133, but the standard deviation of US\$9,184 suggests considerable variation in costs from patient to patient.

DISCUSSION

As the large number of series assessed in this review attests, laparoscopic colectomy for adenocarcinoma is feasible, but the lack of RCTs available has made it difficult to assess the procedure's safety and efficacy compared with the traditional open procedure. Although there appear to be no significant differences between the two procedures in terms of many of the yardsticks used in this review, this does not necessarily imply that any confidence can be placed in a statement of equivalence between the procedures.

This review found no significant differences in terms of overall complication rates, overall recurrence rates, disease-free survival rates, perioperative death rates, or rates of long-term survival. However, to accept the null hypothesis that there is no real difference in any of these factors may be to commit a type 2 error (when the null hypothesis is accepted when it is in fact false). Because of the small sample sizes of many of the studies reviewed here and the inability to combine results into a large meta-analysis, this possibility remains high. For example, to reduce the risk of this type of error, an American National Institutes of Health RCT of laparoscopic colectomies proposes to enroll 1,200 subjects. This subject pool will give the statistical tests sufficient power that equivalence between the two procedures will be concluded with a probability of 0.2% if there is actually a 10% difference in recurrence rates; however, if there is actually a 5% difference in recurrence rates, there remains a probability of 19% that equivalence will be assumed.⁵

It seems safe to conclude from the studies reviewed here that LARCM takes significantly longer to perform. It also seems likely that it incurs significantly higher medical costs, although the evidence base is thin in this regard. There is also some possibility that the procedure is associated with increased surgical stress, possibly as a result of the increased duration of surgery, although the evidence base is too narrow and more studies would appear to be required to answer this question. However, LARCM undeniably results in improved cosmesis and is associated with quicker hospital discharge and less narcotic use, although this last benefit may attach to some types of colectomies more than others. There is also evidence that it also results in less pain when at rest, at least for patients for whom the surgery is successfully completed, and an earlier return of bowel function and hence normal diet. These conclusions are summarized in Table 15.

The disadvantages identified for LARCM appear to group together around the trend toward increased duration of surgery. Longer operating times are associated with in-

Table 15. ADVANTAGES AND DISADVANTAGES OF LAPAROSCOPIC VERSUS OPEN COLECTOMY

Advantages	Disadvantages
Improved cosmesis*	Significantly longer operative times
Quicker hospital discharge	Possibly more expensive
Less narcotic use, though possibly larger benefits for certain types of colectomy (i.e. low colonic procedures)	Possibly worse short-term immune effects
Possibly less pain at rest, at least for patients who have unconverted laparoscopic procedures	
Possibly earlier return of bowel function and resumption of normal diet	

* No data for this conclusion, but appears uncontentious.

creased costs, although other factors such as disposable instruments also contribute significantly toward this. Longer operating times are also correlated with increasing surgical stress, and although the notion of laparoscopic surgery producing more surgical trauma than open techniques appears to run counter to experience with surgical procedures other than colectomies, it is a possibility. However, this observation should not be overemphasized, based as it is on a restricted data set of cancer colectomies alone; it would also appear to be contentious because it directly contradicts the results of other studies that have examined the immune and stress effects associated with laparoscopic surgery in general. Harmon et al,⁶¹ for instance, found a significant blunting of the IL-6 response associated with laparoscopic colectomy (for benign and malignant disease) compared with open surgery, and other authors when reviewing the broader literature have also remarked on the benefits of laparoscopic surgery in reducing trauma.^{62–64} Given the limited and contradictory data available, it would appear to be premature to make any inferences about the stress and immunologic effects of laparoscopic colectomy for the treatment of adenocarcinoma.

Specifically with reference to port and wound site recurrences, this review found that rates were not significantly different from wound recurrence rates reported in series of open colectomies. This review found a rate of 1.28% (95% CI 0.64–2.27), which compares favorably with those of the two previously mentioned open series, namely 0.81% (95% CI 0.43–1.38)²⁶ and 0.64% (95% CI 0.32–1.15).²⁷ It is also in line with a recent review of port site risk, which found a laparoscopic rate of 0.85% (95% CI 0.14–1.18).²⁸ This last review included studies (or partial data) that would have been excluded by this review's protocol. However, this reinforces the suggestion that earlier reports of more alarming rates of laparoscopic port site implantation may have had more

to do with surgeon inexperience and the development of new techniques than with inherent risks of the procedure.

In contrast, the advantages associated with LARCM are precisely some of those that were extrapolated from experience with laparoscopic cholecystectomy and, apart from improved cosmesis, are all associated with immediate postoperative gains. Because there is little suggestion that LARCM results in superior cancer outcomes compared with open procedures, the question becomes whether the improvement in cosmesis and these other short-term advantages outweigh the possible disadvantages attendant on the increased operating time associated with this new procedure.

The Council of the Royal Australasian College of Surgeons endorsed the following ASERNIP-S safety and efficacy classification for LARCM: "The safety and/or efficacy of the procedure cannot be determined at the present time due to an incomplete and/or poor-quality evidence base. It is recommended that further research be conducted to establish safety and/or efficacy." Specifically, because of concerns regarding a lack of evidence detailing circumferential marginal clearance of tumors in the rectum and ascending and descending colon and the need to determine a precise incidence of cardiac and other major complications, along with wound and port site recurrence, it is recommended that a controlled clinical trial, ideally with random allocation to an intervention and control group, be conducted. Long-term survival rates also need to be assessed clearly. The proposed multicenter Australian trial of LARCM would be a suitable vehicle to evaluate all of these variables. Because of its similar protocol to the large American NIH study underway, a meta-analysis will be possible of the combined data and a definitive picture can be made of the relative risks of laparoscopic-assisted resection and traditional open resection of colorectal malignancies

References

- Tomita H, Marcelo PW, Milsom JW. Laparoscopic surgery of the colon and rectum [review]. *World J Surg* 1999; 23:397–405.
- Ota DM, Nelson H, Weeks JC. Controversies regarding laparoscopic colectomy for malignant diseases. *Curr Opin Gen Surg* 1994; 208–213.
- Milsom JW, Kim SH. Laparoscopic versus open surgery for colorectal cancer. *World J Surg* 1997; 21:702–705.
- Holzman MD, Eubanks S. Laparoscopic colectomy. Prospects and problems. *Gastrointest Endosc Clin North Am* 1997; 7:525–539.
- Stocchi L, Nelson H. Laparoscopic colectomy for colon cancer: trial update [review]. *J Surg Oncol* 1998; 68:255–267.
- Luck A, Hensman C, Hewett P. Laparoscopic colectomy for cancer: a review. *Aust NZ J Surg* 1998; 68:318–327.
- Leichter RF, Welton ML. Laparoscopic colectomy. *Semin Gastrointest Dis* 1994; 5:140–145.
- Wexner SD, Cohen SM. Port site metastases after laparoscopic colorectal surgery for cure of malignancy. *Br J Surg* 1995; 82:295–298.
- Australian Institute of Health, Welfare (AIHW), Australasian Association of Cancer Registries (AACR). *Cancer in Australia 1995: Incidence and mortality data for 1995 and selected data for 1996*. Cancer series No. 10. Canberra: Australian Institute of Health and Welfare; 1998.

10. Ota DM. Colon cancer. *Cancer Treat Res* 1997; 90:347–356.
11. Bertagnolli MM, Mahmoud NN, Daly JM. Surgical aspects of colorectal carcinoma. *Hematol Oncol Clin North Am* 1997; 11:655.
12. Wexner SD, Latulippe JF. Laparoscopic colorectal surgery and cancer. *Dig Surg* 1998; 15:117–123.
13. Tilsed JVT. Recent advances in surgery for colorectal cancer [review]. *Crit Rev Oncol Hematol* 1999; 30:201–205.
14. Guillou PJ. Laparoscopic colectomy. *Curr Pract Surg* 1994; 6:190–193.
15. Mathis CR, MacFadyen BV. Laparoscopic colorectal resection: a review of the current experience. *Int Surg* 1994; 79:221–225.
16. Monson JT, Hill AK, Darzi A. Laparoscopic colonic surgery [review]. *Br J Surg* 1995; 82:150–157.
17. Berman IR. Laparoscopic resection for colon cancer: cause for pause. *Important Adv Oncol* 1996; 231–243.
18. Bertagnolli MM, DeCosse JJ. Laparoscopic colon resection for cancer: an unfavorable view. *Adv Surg* 1996; 29:155–164.
19. Ramshaw BJ. Laparoscopic surgery for cancer patients. *CA Cancer J Clin* 1997; 47:327–350.
20. Savalgi RS. Port-site metastasis in the abdominal wall: fact or fiction [review]. *Semin Surg Oncol* 1998; 15:189–193.
21. Paik PS, Beart RW. Laparoscopic colectomy. *Surg Clin North Am* 1997; 77:1.
22. Bouvy ND, Marquet RL, Jeekel H, Bonjer HJ. Impact of gas(less) Laparoscopy and laparotomy on peritoneal tumor growth and abdominal wall metastases. *Ann Surg* 1996; 224:694–701.
23. Cook TA, Dehn TC. Port-site metastases in patients undergoing laparoscopy for gastrointestinal malignancy. *Br J Surg* 1996; 83:1419–1420.
24. Nduka CC, Monson JR, Menzies GN, Darzi A. Abdominal wall metastases following laparoscopy. *Br J Surg* 1994; 81:648–652.
25. Bertagnolli MM, DeCosse JJ. Laparoscopic colectomy for cancer [editorial]. *J Surg Oncol* 1995; 58:211.
26. Hughes ESR, McDermott FT, Polglase AL, Johnson WR. Tumor recurrence in the abdominal wall scar tissue after large-bowel cancer surgery. *Dis Colon Rectum* 1983; 26:571–572.
27. Reilly WT, Nelson H, Schroeder G, et al. Wound recurrence following conventional treatment of colorectal cancer: a rare but perhaps underestimated problem. *Dis Colon Rectum* 1996; 39:200–207.
28. Allardyce RA. Is the port site really at risk? Biology, mechanisms and prevention: a critical view. *Aust NZ J Surg* 1999; 69:479–485.
29. Kim SH, Milsom JW. Is laparoscopic technique oncologically appropriate for colorectal cancer surgery? *J Korean Med Sci* 1998; 13:227–233.
30. Young-Fadok TM, Talac R, Nelson HUS. Laparoscopic colectomy for cancer: the need for trials. *Semin Colon Rectal Surg* 1999; 10:94–101.
31. Hewitt PM, Ip SM, Kwok SP, et al. Laparoscopic-assisted vs. open surgery for colorectal cancer: comparative study of immune effects. *Dis Colon Rectum* 1998; 41:901–909.
32. Leung KL, Kwok SY, Lau WY, et al. Laparoscopic-assisted resection of rectosigmoid carcinoma: immediate and medium-term results. *Arch Surg* 1997; 132:761–764.
33. Stage JG, Schulze S, Moller P, et al. Prospective randomized study of laparoscopic versus open colonic resection for adenocarcinoma. *Br J Surg* 1997; 84:391–396.
34. Bokey EL, Moore JW, Chapuis PH, Newland RC. Morbidity and mortality following laparoscopic-assisted right hemicolectomy for cancer. *Dis Colon Rectum* 1996; 39:S24–28.
35. Franklin ME, Rosenthal D, Abrego MD, et al. Prospective comparison of open vs. laparoscopic colon surgery for carcinoma. Five-year results. *Dis Colon Rectum* 1996; 39:S35–46.
36. Khalili TM, Fleshner PR, Hiatt JR, et al. Colorectal cancer: comparison of laparoscopic with open approaches. *Dis Colon Rectum* 1998; 41:832–838.
37. Bokey EL, Moore JW, Keating JP, et al. Laparoscopic resection of the colon and rectum for cancer. *Br J Surg* 1997; 84:822–825.
38. McCall JL, Parry BR. Prospective randomized study of laparoscopic versus open colonic resection for adenocarcinoma [letter]. *Br J Surg* 1997; 84:1174.
39. Lacy AM, Delgado S, Garciavaldecasas JC, et al. Port site metastases and recurrence after laparoscopic colectomy: a randomized trial. *Surg Endosc* 1998; 12:1039–1042.
40. Philipson BM, Bokey EL, Moore JE, et al. Cost of open versus laparoscopically assisted right hemicolectomy for cancer. *World J Surg* 1997; 21:214–217.
41. Moore JE, Bokey EL, Newland RC, Chapuis PH. Lymphovascular clearance in laparoscopically assisted right hemicolectomy is similar to open surgery. *Aust NZ J Surg* 1996; 66:605–607.
42. Lacy AM, Garcia VJ, Pique JM, et al. Short-term outcome analysis of a randomized study comparing laparoscopic vs open colectomy for colon cancer. *Surg Endosc* 1995; 9:1101–1105.
43. Kim SH, Milsom JW, Gramlich TL, et al. Does laparoscopic vs. conventional surgery increase exfoliated cancer cells in the peritoneal cavity during resection of colorectal cancer? *Dis Colon Rectum* 1998; 41:971–977.
44. Leung KL, Meng WCS, Lee JFY, et al. Laparoscopic-assisted resection of right-sided colonic carcinoma: a case-control study. *J Surg Oncol* 1999; 71:97–100.
45. Hoffman GC, Baker JW, Doxey JB, et al. Minimally invasive surgery for colorectal cancer: initial follow-up. *Ann Surg* 1996; 223:790–796.
46. Molenaar CH, Bijnen AB, Deruiter P. Indications for laparoscopic colorectal surgery: results from the medical centre Alkmaar, The Netherlands. *Surg Endosc* 1998; 12:42–45.
47. Quattlebaum JK, Flanders HD, Usher CH. Laparoscopically assisted colectomy. *Surg Laparosc Endosc* 1993; 3:81–87.
48. Delgado F, Bolufer JM, Grau E, et al. Laparoscopic colorectal cancer resection, initial follow-up results. *Surg Laparosc Endosc* 1999; 9:91–98.
49. Ramos JM, Gupta S, Anthone GJ, et al. Laparoscopy and colon cancer: is the port site at risk? A preliminary report. *Arch Surg* 1994; 129:897–899.
50. Vukasin P, Ortega AE, Greene FL, et al. Wound recurrence following laparoscopic colon cancer resection. Results of the American Society of Colon and Rectal Surgeons Laparoscopic Registry. *Dis Colon Rectum* 1996; 39:S20–23.
51. Goh YC, Eu KW, Seowchoen F. Early postoperative results of a prospective series of laparoscopic vs. open anterior resections for rectosigmoid cancers. *Dis Colon Rectum* 1997; 40:776–780.
52. Tate JT, Kwok S, Dawson JW, et al. Prospective comparison of laparoscopic and conventional anterior resection. *Br J Surg* 1993; 80:1396–1398.
53. Buchmann P, Christen D. Pro laparoscopic surgery for colorectal cancer. *Dig Surg* 1995; 12:296–301.
54. Delgado F, Bolufer JM, Grau E, et al. Early results of laparoscopic resection of colorectal cancer. *Rev Esp Enferm Dig* 1998; 90:329–334.
55. Leung KL, Yiu RYC, Lai PBS, et al. Laparoscopic-assisted resection of colorectal carcinoma: five-year audit. *Dis Colon Rectum* 1999; 42:327–332.
56. Vara-Thorbeck TC, Garcia CM, Salvi M, et al. Indications and advantages of laparoscopy-assisted colon resection for carcinoma in elderly patients. *Surg Laparosc Endosc* 1994; 4:110–118.
57. Fukushima R, Kawamura YJ, Saito H, et al. Interleukin-6 and stress hormone responses after uncomplicated gasless laparoscopic-assisted and open sigmoid colectomy. *Dis Colon Rectum* 1996; 39:Suppl. S.
58. Konishi F, Nagai H, Kashiwagi H, et al. Laparoscopy-assisted colectomy with extracorporeal anastomosis. *Dig Endoscop* 1994; 6:52–58.
59. Lord SA, Larach SW, Ferrara A, et al. Laparoscopic resections for colorectal carcinoma: a three-year experience. *Dis Colon Rectum* 1996; 39:148–154.

60. Van Ye TM, Cattey RP, Henry LG. Laparoscopically assisted colon resections compare favorably with open technique. *Surg Laparosc Endosc* 1994; 4:25–31.
61. Harmon GD, Senagore AJ, Kilbride MJ, Warzynski MJ. Interleukin-6 response to laparoscopic and open colectomy. *Dis Colon Rectum* 1994; 37:754–759.
62. Lee SW, Whelan RLU. The immunologic effects of laparoscopic colectomy. *Semin Colon Rectal Surg* 1999; 10:74–84.
63. Whelan RL, Allendorf JD, Gutt CN, et al. General oncologic effects of the laparoscopic surgical approach. 1997 Frankfurt International Meeting of Animal Laparoscopic Researchers. *Surg Endosc* 1998; 12:1092–1095.
64. Paik PS, Beart RW. Laparoscopic colectomy. *Surg Clin North Am* 1997; 77:1.
65. Neuhaus SJ, Texler M, Hewett PJ, Watson DI. Port-site metastases following laparoscopic surgery [review]. *Br J Surg* 1998; 85:735–741.
66. National Health, Medical Research Council. A designation of levels of evidence. Guide to the development, implementation and evaluation of clinical practice guidelines 1999; Appendix B:52.
67. Gellman L, Salky B, Edye M. Laparoscopic-assisted colectomy. *Surg Endosc* 1996; 10:1041–1044.
68. Musser DJ, Boorse RC, Madera F, Reed JF. Laparoscopic colectomy: at what cost? *Surg Laparosc Endosc* 1994; 4:1–5.
69. Baca I, Gotzen V, Petricevic M, Petricevic A. Laparoscopy-assisted colorectal surgery. *Croat Med J* 1996; 37:169–173.
70. Cohen SM, Wexner SD. Laparoscopic colorectal resection for cancer: the Cleveland Clinic Florida experience. *Surg Oncol* 1993; 2:1–42.
71. Dean PA, Beart RW, Nelson H, et al. Laparoscopic-assisted segmental colectomy: early Mayo Clinic experience. *Mayo Clin Proc* 1994; 69:834–840.
72. Guillou PJ, Darzi A, Monson JR. Experience with laparoscopic colorectal surgery for malignant disease. *Surg Oncol* 1993; 2(suppl 1):43–49.
73. Jacobs M, Verdeja JC, Goldstein HS. Minimally invasive colon resection (laparoscopic colectomy). *Surg Laparosc Endosc* 1991; 1:144–150.
74. Zucker KA, Pitcher DE, Martin DT, Ford RS. Laparoscopic-assisted colon resection. *Surg Endosc* 1994; 8:12–17.