ΜΕΤΑΠΤΥΧΙΑΚΟ ΠΡΟΓΡΑΜΜΑ ΣΠΟΥΔΩΝ:

‘‘ΕΛΑΧΙΣΤΑ ΕΠΕΜΒΑΤΙΚΗ ΧΕΙΡΟΥΡΓΙΚΗ,

ΡΟΜΠΟΤΙΚΗ ΧΕΙΡΟΥΡΓΙΚΗ ΚΑΙ ΤΗΛΕΧΕΙΡΟΥΡΓΙΚΗ’’

ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ

ΙΑΤΡΙΚΗ ΣΧΟΛΗ

ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

ΘΕΜΑ:

LAPAROSCOPIC COLECTOMY. A REVIEW OF LITERATURE

ΜΕΤΑΠΤΥΧΙΑΚΟΣ ΦΟΙΤΗΤΗΣ:

ΓΚΑΡΑΒΕΛΛΑΣ Π. ΓΕΩΡΓΙΟΣ

Α.Μ.: 20110788

ΑΘΗΝΑ, ΜΑΡΤΙΟΣ 2015

ΠΡΑΚΤΙΚΟ ΚΡΙΣΕΩΣ

ΤΗΣ ΣΥΝΕΔΡΙΑΣΗΣ ΤΗΣ ΤΡΙΜΕΛΟΥΣ ΕΞΕΤΑΣΤΙΚΗΣ ΕΠΙΤΡΟΠΗΣ

ΓΙΑ ΤΗΝ ΑΞΙΟΛΟΓΗΣΗ ΤΗΣ ΔΙΠΛΩΜΑΤΙΚΗΣ ΕΡΓΑΣΙΑΣ

Του Μεταπτυχιακού Φοιτητή Γκαραβέλλα Π. Γεωργίου

Εξεταστική Επιτροπή

- Ιωάννης Γκρινιάτσος, Αναπλ. Καθηγητής Χειρουργικής **(Επιβλέπων)**
- Χρήστος Π. Τσιγκρής, Καθηγητής Χειρουργικής & Επιστημονικός Υπεύθυνος του Π.Μ.Σ.
- Θεόδωρος Διαμαντής, Καθηγητής Χειρουργικής

Η Τριμελής Εξεταστική Επιτροπή η οποία ορίσθηκε από την ΓΣΕΣ της Ιατρικής Σχολής του Παν. Αθηνών Συνεδρίαση της.....ης ..... 20.... για την αξιολόγηση και εξέταση του υποψηφίου κου Γκαραβέλλα Π. Γεωργίου, συνεδρίασε σήμερα .../.../....

Η Επιτροπή διαπίστωσε ότι η Διπλωματική Εργασία του Κου Γκαραβέλλα Π. Γεωργίου με τίτλο: **LAPAROSCOPIC COLECTOMY. A REVIEW OF LITERATURE**, είναι πρωτότυπη, επιστημονικά και τεχνικά άρτια και η βιβλιογραφική πληροφορία ολοκληρωμένη και εμπεριστατωμένη.

Η εξεταστική επιτροπή αφού έλαβε υπ' όψιν το περιεχόμενο της εργασίας και τη συμβολή της στην επιστήμη, με ψήφους ..... προτείνει την απονομή του Μεταπτυχιακού Διπλώματος Ειδίκευσης (Master's Degree), στον παραπάνω Μεταπτυχιακό Φοιτητή.

Στην ψηφοφορία για την βαθμολογία ο υποψήφιος έλαβε για τον βαθμό «ΑΡΙΣΤΑ» ψήφους ....., για τον βαθμό «ΛΙΑΝ ΚΑΛΩΣ» ψήφους ....., και για τον βαθμό «ΚΑΛΩΣ» ψήφους ..... Κατά συνέπεια, απονέμεται ο βαθμός «.....».

Τα Μέλη της Εξεταστικής Επιτροπής

- Ιωάννης Γκρινιάτσος, **(Επιβλέπων)** (Υπογραφή) ———————

- Χρήστος Π. Τσιγκρής, (Υπογραφή) ———————

- Θεόδωρος Διαμαντής, (Υπογραφή) ———————

CONTENTS

1. Introduction

Colorectal cancer is the second leading cause of cancer-related death in western countries. Adequate surgical resection is the only curative treatment, with overall survival rates of just under 50% at 5 years. The surgical technique is critical, with respect to both cure and local recurrence. Rates of complications and death from standard colon cancer surgery have been reported to range from 8% to 15% and 1% to 2%, respectively. [1-3]

Three main methods are currently used to perform a colorectal resection: the traditional "open" technique via laparotomy, the laparoscopic approach and a hybrid hand-assisted laparoscopic approach, using a device that allows the surgeon access through a mini laparotomy incision while maintaining the pneumoperitoneum. As more evidence from randomized trials demonstrating the efficacy and safety of the laparoscopic approach becomes available,[4,5] surgeons are increasingly pressured to offer minimally invasive procedures to patients with both benign and malignant colorectal pathology.

In 1991, Jacobs *et al*. reported the first series of laparoscopic colonic resection in 20 patients.[6] After this initial study, many other authors have reported on the use of laparoscopic approach for a variety of benign colorectal conditions. However, laparoscopic colectomy had not been accepted as quickly as laparoscopic cholecystectomy. This was because of its steep learning curve, concerns with oncological outcomes, absence of randomized controlled trials (RCTs) and early reports of port-site recurrence after curative cancer resection. [7] The first RCT looking at late outcomes of laparoscopic surgery for colonic cancer was reported by Lacy *et al*. [8]

Initially, Laparoscopic Colon Resection (LCR) was slow to gain acceptance. In 2002, only 8% of all colon resections were performed laparoscopically and 7% to 9% were performed using a hand-assisted laparoscopic approach. [9] In the current era of evidenced-based medicine, enthusiasm for laparoscopic colorectal surgery is rapidly gaining momentum.

2. Indications for Laparoscopic Colectomy

The indications for laparoscopic colectomy are essentially the same as the indications for an open procedure, and can be subgrouped into colectomy for benign disease vs neoplasia. ***Benign disease***: This includes inflammatory bowel disease (ulcerative colitis and Crohn's disease), diverticular disease, rectal prolapse, and colonic dysmotility. ***Neoplasia***: This includes polyps not amenable to colonoscopic resection, colorectal cancers, and hereditary colon cancer syndromes such as familial adenomatous polyposis, hereditary non-polyposis colorectal cancer (HNPCC), among others.

3. Potential Benefits of Laparoscopic Colectomy

Several randomized and non-randomized trials have demonstrated the potential benefits associated with laparoscopic colectomy.

3.1. Short-Term Benefits

Less postoperative pain: Most studies have shown a decrease in both the dose and duration of parenteral analgesia required after laparoscopic surgery. These differences are small but not insignificant.[10-11]

Return of bowel function: The majority of trials show that on average, both time to flatus and bowel movement are a day earlier in laparoscopic surgery than open surgery. This also translates into earlier resumption of oral intake.[11]

Shorter hospital stay: The overall hospital stay is decreased by 1 to 2 days for laparoscopic surgery for the reasons mentioned previously.[10-11]

Morbidity and mortality: Three randomized trials found no difference in morbidity and mortality between laparoscopic and open colectomy groups.[10-12]

Average blood loss: This variable has not been consistently reported on across trials, with some reporting less blood loss associated with the laparoscopic-assisted procedure and others reporting no difference in blood loss for the laparoscopic approach. The reduction in blood loss reported is approximately 100 cc. [12]

Cost: Data on a subset of patients (n = 682) in the CLASICC (Conventional vs Laparoscopic Assisted Surgery in patients with Colorectal Cancer) trial were analyzed. [13] The operating room costs associated with the laparoscopic approach were higher than for open colectomy. However, some of this expense was offset by reduced

postoperative cost. The short-term cost analysis showed that the cost associated with laparoscopic surgery was only marginally higher than open surgery (6899 pounds vs 6631 pounds). Similarly, short-term costs were also analyzed for the COLOR trial. [14] Total costs to society did not differ significantly between laparoscopic and open colectomy groups, even though the cost of operation was significantly higher for the laparoscopic vs open approach.

3.2. Long-Term Benefits

Margins and lymphadenectomy: There is no difference in the number of lymph nodes resected and resection margins between laparoscopic and open colectomy. In the COST trial, no difference was present in the median length of bowel margins between laparoscopic and open colectomies.[10] Similarly, the number of lymph nodes removed was also not different between the 2 approaches. [12]

Recurrence rate: Earlier case reports and case series cited a very high rate of port site recurrence for the laparoscopic approach.[14] This resulted in some trepidation in embracing laparoscopic surgery for the treatment of colon cancer, but larger randomized trials did not support this finding. [10-12] In the COST trial, the wound recurrence rate was 0.5% for the laparoscopic group and 0.2% for the open group.[10] Local recurrence rates were also similar between the 2 groups. [10,12]

Survival: No difference in overall survival has been observed between laparoscopic and open surgery. In the COST trial, overall survival was similar for the laparoscopic and open surgery groups at 3 years with any stage of cancer. [10] Lacy and colleagues[12] found a survival advantage in a subgroup of their patients with stage 3 colon.

Reduced overall cost: Although long-term studies are still lacking, the faster recovery associated with the laparoscopic technique potentially translates into fewer days lost to illness, and decreased overall cost to society. [14]

4. Issues in Bowel Preparation

Bowel preparation before colorectal surgery is still commonly recommended and performed in many centers in the United States. Earlier patient series reported complications such as anastomotic dehiscences, intra-abdominal sepsis, and wound infection as the most common cause of postoperative mortality. [15] The higher rate of these complications was attributed to higher degrees of intestinal contamination.

Although current clinical data offer no evidence to support the claim that preoperative colon cleansing reduces the risk of anastomotic leaks or infectious complications [16], preoperative bowel preparation is used by many surgeons during laparoscopy because it adds to the ease of bowel handling and potentially reduces operative time. During laparoscopy the palpation of colorectal lesions is very difficult, therefore a clean colon can aid in identification of a lesion.

5. Equipment [17]

Operating Table: An electronically operated table is preferable for the frequent changes in position needed for laparoscopic colectomy

Video Equipment: The necessary video equipment to replace the surgeon's direct visual perception and provide an image of the surgical field for safe laparoscopic surgery includes a video camera unit, the laparoscope, a light source, and monitoring and recording devices.

Insufflators: A high-flow insufflator capable of delivering at least 10 liters/min of gas is needed to establish and maintain a pneumoperitoneum to effectively perform laparoscopic colectomy.

Irrigation and Suction Devices: During advanced laparoscopic surgery a reliable combination irrigation-suction system is necessary to both irrigate rapidly and to effectively evacuate fluid or other material.

Electrocautery: Monopolar electrocautery is commonly connected to dissecting instruments and scissors to assist with surgical dissection and provide haemostasis for small vessels.

Instruments: Because there is limited access to the surgery site during laparoscopic surgery, instruments are key to assist the surgeon in the operation. There are many similar instruments currently available from different manufacturers to fulfil the purposes of laparoscopic colorectal surgery. The design of laparoscopic instruments is important: they must be of adequate length, light, easy to manipulate, easy to visualize via the laparoscopic view, and be able to rotate 360°. It is also important that the instrument can be easily manipulated with a surgeon's single hand. In the current climate of cost containment and possible disease transmission, controversial issues continue to be discussed relative to the less expensive reusable versus the more expensive disposable instruments. Continued modification and new designs of

instruments are important to promote the advances of laparoscopic surgery. The basic requirements of laparoscopic instrumentation can be divided into four main categories:

1. *Instruments to establish and maintain pneumoperitoneum and to provide entry ports for surgical instruments*
2. *Instruments for tissue dissection and mobilization*
3. *Instruments for resection and anastomosis*
4. *Other specialized instruments for laparoscopic colorectal surgery.*

6. Laparoscopic Right Colectomy[18]

The patient is placed supine. A Trendelenburg position is required at the initial stage of the operation with some left rotation. The surgeon stands to the left of the patient, and the first assistant to the surgeon's left. The second assistant is positioned between the patient's legs.

The Recommended Instruments are:

- Two 10-mm trocars
- Three 5-mm trocars
- A 12-mm trocar with reducer
- Three 5-mm fenestrated grasping forceps
- Five-millimetre coagulating shears
- A 5-mm straight grasping forceps
- A 5- or 10-mm harmonic scalpel
- A 10-mm fenestrated forceps
- A 10-mm curved dissector
- A 5-mm needle holder
- A 12-mm linear stapler
- A 0° endoscope

A pneumoperitoneum is performed using the Veress needle. A 10-mm para-umbilical trocar for the 0° scope is inserted. Two trocars, one 5-mm suprapubic and

the other 12-mm supra-umbilical, will enable the positioning of working instruments for both hands. Two 5-mm right iliac fossa and right subcostal trocars will be used for the exposure instruments. The caecum is grasped with a Johann fenestrated forceps. The patient is placed in a 20° Trendelenburg position with left lateral rotation. The small bowel is placed in the upper part of the peritoneal cavity. Dissection starts with the coagulating scissors or harmonic scalpel. The posterior parietal peritoneum is opened, after checking for the right ureter. The right mesocolon is detached from the right renal fascia to the duodenal genus inferius. Right parietal colonic detachment is continued with complete release of the parietal attachments.

The patient is now placed in a slightly prone position. The transverse colon and the greater omentum are exposed. The omental attachments of the transverse colon are released using the coagulating shears or harmonic scalpel. Proper dissection frees the genus superius. The ligaments of the hepatic flexure are dissected. The two lower and upper dissection planes then communicate. The right colon and mesocolon are completely freed.

The patient is left in the same position. Exposure of the ileocecal junction is initially performed through the suprapubic and subcostal trocars. The colon is now under traction by the two exposure instruments. Mesenteric fenestration on both sides of the ileocaecal vessels is performed. The vessels are controlled either by an intracorporeal ligature or by vascular linear stapling. Second, the right colic vessels are exposed at the anterior part of the head of the pancreas, respecting Henlι's gastrocolic venous trunk. Transverse mesocolic fenestration makes it possible to isolate precisely the vascular pedicle before ligature or stapling. An additional omental resection is done.

The surgeon moves to the patient's right side at this step. A small, up-to-5-cm lateral incision is made in the right lower quadrant. The wound is protected with a plastic sheet. The prepared colon is extracted. The paracolic vessels are controlled with conventional ligature. Ileal and colic resection is carried out.

A hand-sewn, or stapled latero-lateral anastomosis with two firings is done. The bowel is put back into the peritoneal cavity. The incision is closed with care.

7. Laparoscopic Left Colectomy[18]

The patient is placed supine, with a 20° Trendelenburg position. The surgeon and the first assistant stand to the right of the patient. The second assistant is positioned between the legs of the patient. The video monitor is on the patient's left side.

The Recommended Instruments are:

- Two 10-mm trocars
- Three 5-mm trocars
- A 12-mm trocar with reducers
- Three 5-mm fenestrated grasping forceps
- A 5-mm coagulating shears
- A 5-mm straight grasping forceps
- Harmonic scalpel, 5 or 10 mm
- A 10-mm fenestrated forceps
- A 10-mm dissector
- A 5-mm needle holder
- Twelve-millimetre linear staplers
- A circular stapler for the anastomosis
- A 0° endoscope
- A parietal protective drape with an opening of 7 cm

The pneumoperitoneum is created with a Veress needle. The first trocar for the endoscope is inserted laterally, about 5 cm to the right of the umbilicus. The other trocars are then introduced under direct vision. A 5-mm trocar is placed suprapubic, a 12-mm trocar in the right iliac fossa, and a 10-mm trocar with reducer at the lower margin of the umbilicus. Two extra trocars will be needed at the time of splenic flexure mobilization. The abdominal cavity is visually explored as a 20°

Trendelenburg position is installed. The grasping forceps inserted through the suprapubic port mobilizes the omentum, the transverse colon and the small bowel. The rectosigmoid junction is then exposed using the suprapubic instrument.

The secondary attachments of the sigmoid mesocolon are transected using the coagulating shears or the harmonic scalpel. The left ureter is identified. The suprapubic forceps mobilizes the rectosigmoid junction to the left side of the patient. The promontorium is easily identified. The right ureter is outlined and the posterior parietal peritoneum is opened with the harmonic scalpel or the coagulating shears. Dissection is continued in the pre-sacral region in contact with the mesorectal fat. The suprapubic fenestrated instrument applies vertical traction on the inferior mesenteric vessels. The dissection is continued along the inferior edge of the inferior mesenteric pedicle to its origin. A retromesenteric window is made. The left ureter is recognized once again in this freed space. The inferior mesenteric vessels can be controlled with a linear stapler or with intracorporeal ligature or clipping.

The position of the trocars is changed. The endoscope is positioned in the umbilical region in the 10-mm trocar. A new 5- or 10-mm trocar is positioned in the left iliac fossa, and a final 5-mm trocar is positioned on the median supraumbilical line. The patient is placed in a reverse Trendelenburg position. The small bowel is re-positioned in the pelvic cavity. The coloparietal attachments are kept at this stage. A left retromesocolic dissection is carried out. The left mesocolon is lifted by the suprapubic instrument. The harmonic scalpel or the coagulating scissors inserted through the left iliac fossa port enable opening of the left retrocolic sub-peritoneal space up to the splenic flexure, and reaching the lower edge of the pancreas. The lesser sac is opened anteriorly to the pancreas. Thus, the resection of the retroperitoneal attachments of the splenic flexure of the colon is easily carried out.

The inferior mesenteric vein is transected at its termination in an enlarged left colectomy, or somewhat lower depending on the level of the left colic resection. The freeing of the left parietocolic peritoneal attachments is continued using the harmonic scalpel. The whole splenic flexure is thus lowered. The gastrocolic ligament can now be released. The omentum and the transverse colon are exposed using the suprapubic forceps and the supraumbilical instrument. The colo-omental attachments are released with the harmonic scalpel or the coagulating shears. The left colon is then totally released from its parietal attachments

The patient is placed back as in the beginning of the procedure, and the endoscope goes back into the right lateral trocar. Opening of the left and right posterior parietal peritoneum is continued with the harmonic scalpel and the coagulating shears. Resection of the perirectal peritoneum is continued. The upper rectal wall is outlined. Wide opening of the presacral space is continued posteriorly, respecting the posterior pre-sacral layer. As no complete mesorectal excision is needed in a left colectomy, the level of resection is located in the upper rectum. But the dissection may include total mesorectal excision in case of coloproctectomy. The posterior mesorectum is freed from the rectal tube with a 10-mm fenestrated forceps at the level chosen for rectal transection. The posterior mesorectum is transected either with the harmonic scalpel or the linear stapler. The rectum itself is then transected with a linear stapler introduced in the 12-mm right iliac fossa port. Several firings are required. An angulating stapler is preferred, especially in lower resections.

The proximal transected colon is grasped with the suprapubic forceps. A McBurney type left retrieval incision is made. A protective drape is installed. The proximal colon extraction is helped by the suprapubic instrument. The colon is checked for the level of disease. Mesocolic resection is done at the level of proximal colon resection. Vessels are ligated. The site of colonic resection is prepared. A tension free anastomosis requires 15 cm of colon length outside the abdomen. The colon is transected and the specimen retrieved. An automatic or hand-sewn purse string is performed with 3/0 nylon suture. The colon is cleaned with iodine. The anvil of a circular stapler is introduced and the purse string tightened. The colon is replaced in the peritoneal cavity, and the retrieval wound is closed.

The pneumoperitoneum is resumed and the small bowel is re-positioned. The peritoneal cavity is rinsed with saline. After anal dilatation, the circular stapler is carefully inserted transanally. The rectal stump is perforated, and the anvil is connected. The circular stapler is closed and fired. The stapler is removed, and the tissue doughnuts are inspected. There should be no tension on the anastomosis. A suction drain is inserted through the suprapubic port.

The abdominal cavity is re-inflated. The ileocolic anastomosis is inspected and the proper positioning of the small bowel is checked. The peritoneal cavity is cleaned with saline and checked for bleeding. The mesenteric opening can be sutured at this stage, but can also be missed. A suction drain is left in the right parietal fossa.

8. Laparoscopic Total Colectomy[18]

The patient is placed supine in a 20° Trendelenburg position. The surgeon and first assistant are on the right side of the patient. The second assistant stands between the legs of the patient. The video monitor is placed to the left of the patient.

The Recommended Instruments are:

- A 0° endoscope
- Two 10-mm trocars
- Three 5-mm trocars
- A 12-mm trocar with reducer
- Three 5-mm fenestrated grasping forceps
- A 5-mm coagulating shears
- Three 5-mm straight grasping forceps
- A 5- or 10-mm harmonic scalpel
- A 10-mm fenestrated forceps
- A 10-mm curved dissector
- A 5-mm needle holder
- One 12-mm linear stapler
- One circular stapler
- A plastic protective surgical drape with a 7-cm opening

Total Colectomy with rectal resection is the addition of a Left Colectomy followed by a Right Colectomy.

9. Postoperative Care

Following laparoscopic colon surgery, patients experience an earlier return of gastrointestinal function than those individuals undergoing open surgery. Whether a laparotomy or a laparoscopic resection has been performed, most surgeons remove the

naso- or orogastric tube at the end of the operation. Most patients are able to tolerate an oral diet by the first or second day after surgery and are offered liquids almost routinely the day following surgery. If liquids are tolerated, the diet is rapidly advanced to solids. The rather subjective length of stay has also been shown to decrease by as much as 3 to 5 days following laparoscopic colectomy as compared to laparotomy. Patients undergoing laparoscopic resections have less perceived pain and lower narcotic requirements as compared to patients undergoing laparotomy. Patients undergoing laparoscopic surgery also have equivalent results as compared to laparotomy with regards to perioperative mortality, length of specimen resected, adequacy of margins, and number of lymph nodes collected. Improved postoperative T-cell-mediated immunity, lymphocyte function, and neutrophil chemotaxis have also been seen after laparoscopic surgery.

Return to normal activity is based on each individual patient, depending upon their age, normal occupation, and motivation. Patients should not drive while taking postoperative narcotic medications, and heavy lifting should also be avoided for at least 6 weeks after surgery.

10. Complications

Several series of laparoscopic colectomy have been reported in the literature that have described the numerous complications which can occur with these procedures. For the most part, the same complications associated with laparotomy have also occurred during laparoscopic colectomy; these include ureteral injuries, inadvertent enterotomies, anastomotic leaks, postoperative strictures or even actual obstruction at the anastomosis, herniation through the mesenteric defect, and intra-abdominal abscess. Certain complications, such as port site hernia, are specific to the laparoscopic approach. The overall rate of complications is approximately 9%. Ileus and small bowel obstruction, both operative and non-operative, are the most common causes for readmission (in about 4% of cases). Abdominal abscess and anastomotic leak occur in 1.1% and 0.7% of cases, respectively. Other complications include fever, dehydration, pulmonary embolus, wound infection, and cardiac arrhythmias.

Internal hernias, although commonly reported with other minimally invasive procedures such as Roux-en-Y gastric bypass, are a rare occurrence after laparoscopic colectomy.

11. Learning Curve in Laparoscopic Colorectal Surgery

Laparoscopic colorectal surgery is technically challenging. These procedures include various types of operations that frequently involve two or more abdominal quadrants, control of large blood vessels, identification of extraperitoneal structures such as the ureters, and intra- or extracorporeal reconstruction of intestinal continuity. Moreover, infection and inflammatory processes such as Crohn's disease and diverticulitis may present a hostile environment for the laparoscopic surgeon due to distorted anatomy and handling of friable and inflamed tissue. These factors may affect initial outcome early in the learning curve. The aim of this study was to evaluate the learning curve for these procedures based on the initial outcome of our first 100 elective operations with emphasis on crucial questions such as complications and extent of oncologic resection.

Our overall results are comparable to other reported series in terms of morbidity and short-term outcome[19] and thus can serve as a reliable database for evaluating factors related to the learning curve. The learning curve in laparoscopic colorectal surgery should initially reflect the number of cases needed to conduct these procedures with a reasonable rate of significant complications, and only then should other factors be evaluated. In this series major complications decreased substantially after the first 50 cases. Several other studies have demonstrated the impact of surgeon experience on complications, showing a significant decrease in the complications rate as experience is gained [20-21]. Agachan et al. [21] reported similar results and concluded that at least 50 procedures are necessary to lower the complication rate significantly.

Another study by Bennett and co authors[20] demonstrated fewer complications with surgeons who had performed more than 40 cases. The cumulative intraoperative and postoperative complications were double with the less experienced surgeons (25% vs. 14%). Others have demonstrated the same trend.

Nevertheless, the number of operations is not the only factor influencing the complication rate. Other factors such as general experience in laparoscopic surgery, colonic pathology, and type of procedure play a major role as well. Difficult procedures such as resection of low rectal tumors, severe diverticular disease, and more extensive operations such as subtotal colectomy increase the complication risk [21-22]. A second very important goal is to set and meet primary oncologic goals in

colorectal cancer patients. These goals, as represented by negative surgical margins and adequate number of harvested lymph nodes, can be met early in the learning curve, as demonstrated in our series. This obviously mandates adhering to standard cancer resection techniques as in open surgery [23]. A current recommendation of the American Society of Colon and Rectal Surgeons suggests a prerequisite experience of at least 20 laparoscopic colorectal resections for benign diseases or metastatic colon cancer before using laparoscopy to treat curable disease.

The operative time in laparoscopic colorectal surgery is somewhat longer than in open procedures even in experienced hands (table 1). Nevertheless, operative times do decrease along the learning curve, as shown in our series and others. In our opinion, training residents in laparoscopic colorectal surgery should be implemented only when the attending surgeon masters the procedure (which might take at least 50 cases) and should begin in easier cases such as right colectomy or stoma creation[19].

12. Evaluating the Degree of Difficulty of Laparoscopic Colorectal Surgery

A mail survey of 35 internationally renowned laparoscopic colorectal surgeons from Europe and the United States was conducted, and 28 surgeons returned their completed surveys for a response rate of 80%. The surgeons were selected through personal contact and by using a database of surgeons with recognized expertise in laparoscopic colorectal surgery who have participated in educational activities at the European Institute of Telesurgery. The surgeons were first asked to provide an estimate of their total laparoscopic colorectal experience. They were then asked to rate the overall degree of difficulty of 12 specific laparoscopic colorectal procedures using a scale of 1 to 6 (least to most difficult) previously used and validated by Geis et al.[24]

Each of the 12 rated procedures was then broken down into its 4 essential components: exposure, dissection and isolation of the vascular pedicle, mobilization of the specimen, and anastomosis. Participants in the survey were then asked to rate, using the same scale of 1 to 6 (least to most difficult), the degree of difficulty of each of the above steps for each of the 12 procedures. The results were tabulated and the mean difficulty (complexity) score for each individual step calculated. The survey specifically targeted purely laparoscopic procedures and excluded hand-assisted procedures.

The surgeons rated the following 12 procedures: right colectomy with intracorporeal anastomosis, right colectomy with extracorporeal anastomosis, transverse colectomy, splenic flexure resection, left colectomy, sigmoid colectomy with and without splenic flexure mobilization, anterior rectal resection (anastomosis at upper to midrectal level), low anterior rectal resection (low rectal or coloanal anastomosis), abdominoperineal resection, the Hartmann procedure, and Hartmann reversal. The scores given by each surgeon were then tabulated and the mean difficulty (complexity) score for each procedure was calculated.

Collectively, the polled surgeons had performed around 6335 laparoscopic colorectal procedures. Most of them had performed more than 200 procedures (range, 70-700). The overall difficulty score for each procedure is shown in (Figure 1).

Sigmoid colectomy appears to be the simplest procedure to perform, as it had the lowest mean score of 2.0. Looking at the difficulty scores of each of the individual steps of the procedure, achieving and maintaining adequate exposure scored highest, indicating that it is viewed as the most challenging part of the procedure. Once adequate exposure is achieved, vascular ligation, dissection, and resection were found to be relatively straightforward.

Right colectomy with extracorporeal anastomosis was considered more technically challenging than sigmoid colectomy, with an overall difficulty score of 2.3. Analyzing the individual steps of the procedure, dissection of the vascular pedicle appears to be the most challenging portion of the operation. This is probably related to the intricacies of venous anatomy at the Henle trunk, the junction of the gastroepiploic and middle colic veins at the level of the pancreas, and the proximity of structures, such as the duodenum and the superior mesenteric artery and vein. The level of difficulty increased significantly to 3.9 if the anastomosis was to be done intracorporeally, which explains why most surgeons today shy away from performing the anastomosis intracorporeally

Mobilization of the splenic flexure is challenging because of the requirement for an extensive posterior dissection while preserving the vascular supply to the hind gut via the marginal artery. This dissection is carried out along the plane of the Toldt fascia, avoiding retroperitoneal structures such as the ureter and tail of pancreas, which are both at risk for injury. All colorectal procedures requiring splenic flexure

mobilization scored high difficulty ratings. Splenic flexure resection and transverse colectomy were felt to be two of the most difficult procedures, scoring 4.0 and 4.1, respectively.

The Hartmann procedure is associated with a higher overall difficulty rating (3.0) than sigmoid colectomy (2.0), despite the fact that no anastomosis is performed. *The survey did not explicitly inquire as to the reason for this*: **it is most likely owing to the acute inflammatory process that is often present in cases of complicated diverticular disease, which increases the complexity of the exposure as well as the dissection**. The Hartmann reversal was felt to be one of the most difficult procedures, scoring an overall score of 4.5.

Anterior resections were divided into high anterior rectal resections (anastomosis at or above midrectum) and low anterior rectal resections (anastomosis within 6 cm of the anal verge), and the levels of difficulty were considered to be 3.1 and 4.2, respectively (Wilcoxon $P < .001$). The need to perform a total mesorectal excision laparoscopically and perceived difficulties in stapling the low rectum significantly increase the difficulty of the procedure. Abdominoperineal resections scored a level of difficulty of 3.2.

Analyzing the individual components of high and low anterior rectal resection, exposure (2.7 vs 2.9) and vascular dissection with high ligation of the inferior mesenteric vessels (2.2 vs 2.4) scored similarly, indicating the internal validity of the surveyors' ratings; these steps are virtually identical in the 2 procedures. The difference in the overall difficulty score was mostly the result of the differences in the difficulty rating of rectal mobilization in a high vs low anterior rectal resection (2.9 vs 3.4; Wilcoxon $P = .01$) and of the anastomosis (high vs low anterior rectal resection, 2.5 vs 3.2; Wilcoxon $P = .02$). Abdominoperineal resection scored an overall difficulty score similar to high anterior rectal resection.

Each individual step (exposure, vascular dissection, specimen mobilization, and anastomosis) was analyzed in an attempt to further identify the specific difficulties involved in the performance of each procedure. The exposure step appears to be easiest for right colectomy. This can be explained by the ease of placing and keeping the bowel out of the operative field by tilting the patient to the left side and using head-up tilt, without the need for extensive manipulations. Exposure for sigmoid

colectomy was considered more difficult (difficulty score, 2.5), probably because more manipulations of the bowel are required and there is a tendency for it to fall back into the pelvis. Exposure for transverse colectomy scored highest (3.3, most difficult), owing to the mobile nature of the transverse colon and the frequent need to mobilize both flexures for a tension-free anastomosis.

The vascular dissection step can be performed via a medial or lateral approach, and 22 of the 29 responders (76%) reported that they perform the vascular dissection via a medial approach early in the procedure, prior to colonic mobilization. The vascular approach to the left colon was felt to be relatively straightforward, as judged by the comparatively low scores achieved for this step in left colectomy (2.5), sigmoid colectomy (2.3), and anterior rectal resection (2.2). The vascular approach is similar in these procedures and involves dissection of the inferior mesenteric artery trunk or branches thereof. Vascular dissection of the right colon (3.0) and transverse colon (3.3) were felt to be significantly more difficult (Friedman $P = .02$).

The importance of a good anastomosis cannot be overemphasized in colorectal surgery. Looking at the anastomosis step data, it appears that intracorporeal anastomoses are best suited for left-sided and rectal resections where the circular stapler provides a simple way of re-establishing continuity. For right-sided anastomoses it appears that an intracorporeal anastomosis (difficulty score, 3.9) adds considerable challenges to the procedure, suggesting that an extracorporeal one (difficulty score, 1.3; Wilcoxon $P = .03$) should be used to simplify the procedure and reduce operative time. The same is true for transverse colectomies (4.2 vs 1.9; Wilcoxon $P = .02$).

13. Indications for Conversion to Laparotomy

A review of the operative report, however, usually identified the primary problem precipitating the decision to convert. Murray et al grouped the indications for conversion in 3 categories. Of 47 patients, 15 (31.9%) had their procedure converted for technical problems. In 6 patients, the procedure was converted to a laparotomy because of the development of an uncorrectable respiratory acidosis. Pneumoperitoneum decreases the functional residual capacity of the lung.[25-26] The decrease in the functional residual capacity combined with carbon dioxide absorption can produce substantial respiratory acidosis in patients with limited pulmonary

reserve. Through less reliance on Trendelenburg positioning and improved operative management of these patients by anaesthesiologists, there have been no conversions for respiratory acidosis in the latter half of our experience.

Other technical problems requiring conversion included equipment malfunction, inability to expose and identify the ureter, and 1 instance of incorrect location of a colonic neoplasm. This error was identified after the segment of colon had been mobilized but before it was transected. Five patients listed in the category of "too ambitious" included 2 who had proctocolectomies with an ileal pouch–anal anastomosis and 3 with total abdominal colectomies, previously described. Although these operations were proceeding uneventfully at the time of conversion, the projected time required to complete the procedure was judged to be excessive, precipitating a decision to convert to a laparotomy. All 5 of these patients were from the first quarter of our experience, and this result most likely reflects the consequence of limited experience. There have been no subsequent conversions for this reason. Seven similar procedures have been completed successfully.

Nine patients (19.1%) required conversion to a laparotomy to manage intraoperative complications. Most frequently, this was due to persistent bleeding from a mesenteric or retroperitoneal vessel that could not be adequately managed with laparoscopic techniques. Three patients required conversion for an unintentional enterotomy or cystotomy.

In 23 (48.9%) of the 47 patients, the decision to proceed with a laparotomy was precipitated by findings that were thought to exceed the technical limits of laparoscopic dissection. Five patients undergoing sigmoid colectomy for complications of diverticulitis required conversion because of a large paracolic phlegmon. Despite the fact that 105 patients (52.5%) in our series of 200 had previously undergone a laparotomy, only 5 patients required conversion to laparotomy because of extensive intra-abdominal adhesions. Four of these 5 patients had extensive, dense adhesions obliterating the pelvic cavity following a Hartmann resection for pelvic sepsis.

In 3 patients, conversion to a laparotomy was required because operative exposure and laparoscopic dissection were compromised by the patient's obesity. Obesity increases the technical difficulty of laparoscopic and open surgery. Attempts

to quantify the effects of an unfavourable body habitus on laparoscopic surgery and identify an objective measure that could be applied to patient selection have been unsuccessful. We have evaluated the effects of the body mass index (BMI; defined as the patient's weight in kilograms divided by height in meters squared) on the need for conversion to a laparotomy. Obesity is defined as a BMI of more than 29. The 3 patients in our series whose procedure was converted because of obesity had BMIs of 35, 27, and 26. Whereas all of these indexes are above normal (reference range, 19-24), only 1 patient meets the definition of obesity. The BMI correlated with the need for conversion, however. Of 95 patients, 14 (14.7%) with a BMI of less than 28 required conversion, whereas of 58 patients, 16 (27.6%) with a BMI of less than 29 had their operation converted to an open procedure. This difference is statistically significant ($P<.05$). Furthermore, 25 (53.2%) patients who required conversion had a BMI of less than 29, reflecting the fact that obesity accentuates the technical limitations of laparoscopic dissection.

Ten patients required conversion because of concerns about the ability to complete an adequate cancer resection. This was due to extensive adhesions that compromised exposure, adjacent organ involvement by the tumor, or the presence of a bulky tumor that interfered with exposure and mobilization of the colon and adjacent mesentery.

Although the analysis of data regarding changes in the indications for conversion during our experience is hampered by the small number of cases in individual categories, several interesting observations can be made. As our experience has increased, technical problems have become a less frequent indication for conversion, and factors identified as technical limitations of the method have accounted for an increasing proportion of converted operations. Of 15 patients requiring conversion because of technical problems, 9 were from our initial group of 50 patients. Technical problems accounted for 9 (50%) of the 18 conversions in the first quarter compared with 2 (18%) of the 11 conversions in the last quarter. On the other hand, technical limitations accounted for 7 (39%) of the 13 conversions in the first quarter and 7 (64%) of the 11 converted cases in the latter half of our experience. As we have progressed along the learning curve of our experience, these technical limitations have become the primary factor influencing the need for conversion to a laparotomy.

14. Conversion Rates

Conversion rates of laparoscopic to open colectomy varied widely, from 0% to 46% (Table 2). The highest rates were reported in papers that clearly stated that the series resulted from early experience,[27,28] although early experience was not necessarily associated with high conversion rates.[29] For 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 reviews protocol.

15. Laparoscopic Colectomy in the Elderly[30]

Laparoscopic-assisted colectomy in elderly patients is safe, feasible, and has many benefits over open colectomy. Major abdominal surgery in the either chronologically or physiologically older patient no doubt carries a higher risk of morbidity and mortality. The risk of an operation is directly related to the number of identified comorbid illnesses and the physiologic reserve of a patient. Fortunately, advances in medicine have allowed us to perform many of the operations with a much higher degree of safety. As a result, today age is not a contraindication for major surgery.

Laparoscopic-assisted colectomy in the elderly is another medical advancement that allows us to deliver better care to a frail, higher risk group of patients. It offers significant benefit because it appears to be less physiologically stressful than conventional open laparotomy. Laparoscopy results in a significant advantage for remaining independent after surgery, quicker return of activity level, and a decrease in direct costs when compared with similar patients after open resections. In conclusion, LAC should be strongly considered as the preferred surgical approach in the management of many colorectal diseases for appropriately selected elderly patients. One may never be too old to have a laparoscopic colectomy.

16. Clinical trials

16.1 Lacy et al. Trial[31]

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. The clinical trial of Lacy et al. aimed to compare efficacy of LAC and open colectomy (OC) for the treatment of non-metastatic colon cancer in terms of tumor recurrence and survival. From November, 1993, to July, 1998, all patients with adenocarcinoma of the colon were assessed for entry in this randomized 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. A number of 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 tumor 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 tumors (p=0.04, p=0.02, and p=0.006, respectively).The results revealed that LAC is more effective than OC for treatment of colon cancer in terms of morbidity, hospital stay, tumor recurrence, and cancer-related survival.(figure 2)

16.2 COST Trial[32]

Postoperative outcomes of patients undergoing laparoscopic-assisted colectomy (LAC) have shown modest improvements in recovery but only minimal differences in quality of life (QOL) compared with open colectomy. We therefore sought to assess the effect of LAC on QOL in the short and long term, using individual item analysis of multi-item QOL assessments. QOL variables were analyzed in 449 randomized patients from the COST trial 93-46-53 (INT 0146). Both cross-sectional single-time and change from baseline assessments were run at day 2,

week 2, month 2, and month 18 postoperatively in an intention-to-treat analysis using Wilcoxon rank-sum tests. Stepwise regression models were used to determine predictors of QOL. Of 449 colon cancer patients, 230 underwent LAC and 219 underwent open colectomy. Subdomain analysis revealed a clinically moderate improvement from baseline for LAC in total QOL index at 18 months ($P = 0.02$) as well as other small symptomatic improvements.

Poor preoperative QOL as indicated by a rating scale of ≤ 50 was an independent predictor of poor QOL at 2 months postoperatively. QOL variables related to survival were baseline support ($P = 0.001$) and baseline outlook ($P = 0.01$). Eighteen months after surgery, any differences in quality of life between patients randomized to LAC or open colectomy favored LAC. However, the magnitude of the benefits was small. Patients with poor preoperative QOL appear to be at higher risk for difficult postoperative courses, and may be candidates for enhanced ancillary services to address their particular needs. (Figure 3,4)

16.3 Hong Kong Trial[33]

Although laparoscopic resection of colorectal carcinoma improves post-operative recovery, long-term survival and disease control are the determining factors for its application. We aimed to test the null hypothesis that there was no difference in survival after laparoscopic and open resection for rectosigmoid cancer. From Sept 21, 1993, to Oct 21, 2002, 403 patients with rectosigmoid carcinoma were randomized to receive either laparoscopic assisted (n=203) or conventional open (n=200) resection of the tumor. Survival and disease-free interval were the main endpoints. Patients were last followed-up in March, 2003. Perioperative data were recorded and direct cost of operation estimated. Data were analyzed by intention to treat. The demographic data of the two groups were similar. After curative resection, the probabilities of survival at 5 years of the laparoscopic and open resection groups were 76.1% (SE 3.7%) and 72.9% (4.0%) respectively. The probabilities of being disease free at 5 years were 75.3% (3.7%) and 78.3% (3.7%), respectively.

The operative time of the laparoscopic group was significantly longer, whereas postoperative recovery was significantly better than for the open resection group, but these benefits were at the expense of higher direct cost. The distal margin, the number of lymph nodes found in the resected specimen, overall morbidity and

operative mortality did not differ between groups. Laparoscopic resection of rectosigmoid carcinoma does not jeopardise survival and disease control of patients. The justification for adoption of laparoscopic technique would depend on the perceived value of its effectiveness in improving short-term post-operative outcomes.

16.4 CLASICC Trial[34]

The aim of the current study is to report the long-term outcomes after laparoscopic-assisted surgery compared with conventional open surgery within the context of the UK MRC CLASICC trial. Results from randomized trials have indicated that laparoscopic surgery for colon cancer is as effective as open surgery in the short term. Few data are available on rectal cancer, and long-term data on survival and recurrence are now required. The United Kingdom Medical Research Council Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (UK MRC CLASICC; clinical trials number ISRCTN 74883561) trial study comparing conventional versus laparoscopic-assisted surgery in patients with cancer of the colon and rectum. The randomization ratio was 2:1 in favor of laparoscopic surgery. Long-term outcomes (3-year overall survival [OS], disease-free survival [DFS], local recurrence, and quality of life [QoL]) have now been determined on an intention-to-treat basis. Seven hundred ninety-four patients were recruited (526 laparoscopic and 268 open). Overall, there were no differences in the long-term outcomes. The differences in survival rates were OS of 1.8% (95% CI, -5.2% to 8.8%; P = .55), DFS of -1.4% (95% CI, -9.5% to 6.7%; P = .70), local recurrence of -0.8% (95% CI, -5.7% to 4.2%; P = .76), and QoL (P > .01 for all scales).

Higher positivity of the circumferential resection margin was reported after laparoscopic anterior resection (AR), but it did not translate into an increased incidence of local recurrence. Successful laparoscopic-assisted surgery for colon cancer is as effective as open surgery in terms of oncological outcomes and preservation of QoL. Long-term outcomes for patients with rectal cancer were similar in those undergoing abdominoperineal resection and AR, and support the continued use of laparoscopic surgery in these patients.(Figure 5)

16.5 COLOR Trial[35]

The safety and short-term benefits of laparoscopic colectomy for cancer remain debatable. The multicentre COLOR (COlon cancer Laparoscopic or Open

Resection) trial was done to assess the safety and benefit of laparoscopic resection compared with open resection for curative treatment of patients with cancer of the right or left colon. 627 patients were randomly assigned to laparoscopic surgery and 621 patients to open surgery. The primary endpoint was cancer-free survival 3 years after surgery. Secondary outcomes were short-term morbidity and mortality, number of positive resection margins, local recurrence, port-site or wound-site recurrence, metastasis, overall survival, and blood loss during surgery. Analysis was by intention to treat. Here, clinical characteristics, operative findings, and postoperative outcome are reported.

Patients assigned laparoscopic resection had less blood loss compared with those assigned open resection (median 100 mL [range 0-2700] vs 175 mL [0-2000], $p<0.0001$), although laparoscopic surgery lasted 30 min longer than did open surgery ($p<0.0001$). Conversion to open surgery was needed for 91 (17%) patients undergoing the laparoscopic procedure. Radicality of resection as assessed by number of removed lymph nodes and length of resected oral and aboral bowel did not differ between groups. Laparoscopic colectomy was associated with earlier recovery of bowel function ($p<0.0001$), need for fewer analgesics, and with a shorter hospital stay ($p<0.0001$) compared with open colectomy. Morbidity and mortality 28 days after colectomy did not differ between groups. Laparoscopic surgery can be used for safe and radical resection of cancer in the right, left, and sigmoid colon.

16.6 ALCCaS Trial[36]

Laparoscopy has revolutionized many abdominal surgical procedures. Laparoscopic colectomy has become increasingly popular. The short- and long-term benefits and satisfactory surgical oncological treatment of colorectal cancer by laparoscopic-assisted resection remain topical. The long-term outcomes of all international randomized controlled trials are still awaited, and short-term outcomes are important in the interim. Between January 1998 and April 2005, a multicenter, prospective, randomized clinical trial in patients with colon cancer was conducted. Six hundred and one eligible patients were recruited by 33 surgeons from 31 Australian and New Zealand centers. Patients were allocated to colectomy by either laparoscopic-assisted surgery (n = 294) or open surgery (n = 298). Patient

demographics and secondary end-points, such as operative and postoperative complications, length of hospital stay, and histopathological data, will be presented in this article. Analysis was by intention-to-treat. Survival will be reported only as the study matures. Histopathological parameters were similar between the two groups, except in regard to distal resection margins.

There was no statistically significant difference found in postoperative complications, reoperation rate, or perioperative mortality. Statistically significant differences in quicker return of gastrointestinal function and shorter hospital stay were identified in favor of laparoscopic-assisted resection. A statistically significant increased rate of infective complications was seen in cases converted from laparoscopic-assisted to open procedures but with no difference in reoperation or in-hospital mortality. Laparoscopic-assisted colonic resection gives significant improvements in return of gastrointestinal function and length of stay, with an increased operative time and no difference in the postoperative complication rate.

17. Meta-analysis

An analysis of individual pooled data of 4 trials was performed. This meta-analysis was based on individual patient data focusing on overall and disease-free survival 3 years after randomization. The trial statisticians of the Barcelona, COST, COLOR, and CLASICC trials (W.C.J.H., D.J.S., A.C., H.T., and J.B.) operated under strict confidentiality conditions ruling that data of individual trials were only to be shared among the statisticians of the involved trials. The principal investigators of the 4 trials (H.J.B., H.N., A.M.L., and P.J.G.) only had access to the pooled summary data.

Patients with colon cancer who were randomized before March 1, 2000, within the context of the 4 trials and who had undergone curative surgery were included. The exclusion criteria in this meta-analysis were no surgery, absence of data, other carcinoma, irresectable tumor, presence of benign disease, withdrawn informed consent, and presence of distant metastases. All efforts were made to obtain complete data to at least 3 years after randomization. Disease-free survival and overall survival during the first 3 years following randomization were evaluated and compared between the 2 types of surgery. Follow-up after 3 years of randomization was censored. The following data were collected: age, sex, death, metastatic stage, tumor

stage, date of surgery, date of last follow-up, date of randomization, unique patient identification number, 30-day postoperative or in-hospital mortality, involvement of margins of the resected specimens, treatment allocation (laparoscopically assisted or open), number of resected lymph nodes and lymph node stage, date and type (local, distant, or combined) of first tumor recurrence, and type of performed surgical procedure (laparoscopically assisted, conversion from laparoscopy to open, or open surgery). Tumor staging was based on the TNM staging criteria of the American Joint Committee on Cancer and International Union Against Cancer.[37]

Because some patients had open surgery after they had been randomized to laparoscopic surgery and vice versa, an analysis based on the randomized treatment and another analysis based on the received treatment were performed. Patients who underwent conversion to an open procedure remained in their allocated group for analyses. The numbers of patients excluded from the meta-analysis with the corresponding reasons for exclusion were provided for each trial to confirm that the study populations were similar among the 4 trials.

Disease-free survival was defined as time from randomization to death or recurrent disease. Disease-free survival and overall survival after randomization were assessed using the Kaplan-Meier method. Univariate comparisons between the 2 randomized procedures were performed using the log rank test. Multivariate analysis of these outcomes, including an assessment of heterogeneity of treatment effects among the 4 studies, was performed using a stratified Cox proportional hazards regression model that stratified by study and adjusted for sex, age, and stage. A comparison of the number of lymph nodes harvested during surgery was performed using analysis of variance. In this analysis, the number of lymph nodes was transformed logarithmically to obtain approximate normal distributions. The proportions of positive resection margins and postoperative mortality were compared between procedures using exact conditional logistic regression analysis with stratification by trial and included an assessment of heterogeneity of treatment effects. All P values were 2-sided, and $P<.05$ was considered the limit to denote statistical significance.

The total number of patients randomized before March 1, 2000, was 1765. Of these, 229 (13.0%) were excluded from this analysis, most for presence of distant metastases (46.3%) or benign colon disease (41.5%), with similar patterns in the

laparoscopically assisted and open arms (Figure 1). Data for the remaining 1536 patients (208, 640, 520, and 168 patients in the Barcelona, COST, COLOR, and CLASICC trials, respectively) were analyzed. The laparoscopically assisted arm included 796 patients, and the open arm included 740 patients.

Baseline characteristics were similar in the 2 treatment groups (Figure 6). The mean age was 69 years in both arms, and men were as frequently present as women in each treatment group. The stage distribution was similar in both arms. Stage I disease was present in 27.7%, stage II in 39.8%, and stage III in 31.3% of patients, while data were missing to determine the stage in 1.2% of patients.

The mean ± SD number of lymph nodes found in the laparoscopically resected specimens was 11.8 ± 7.4, while 12.2 ± 7.8 lymph nodes were found in the specimens obtained in open colectomy. Analysis of variance showed that this was not significantly different (P = .40) and that the difference did not significantly vary among the 4 studies.

Data on resection margins were missing in 43 patients (who underwent 20 open and 23 laparoscopic colectomies). Positive resection margins were found in 2.1% of the specimens in the open arm and in 1.3% of the specimens in the laparoscopically assisted arm. This was not significantly different between the 2 groups (common odds ratio for open vs laparoscopically assisted surgery for positivity, 1.8; 95% CI, 0.7-4.5; P = .23).

Conversion of laparoscopic to open surgery occurred in 19.0% of patients. Postoperative mortality was 1.6% in the open arm and 1.4% in the laparoscopically assisted arm (common odds ratio for open vs laparoscopically assisted surgery, 1.3; 95% CI, 0.5-3.4; P = .63).

Analysis according to randomized treatment showed that disease-free survival (P = .83) and overall survival (P = .56) for all stages combined after laparoscopically assisted or open resection did not differ. Three-year disease-free survival in the open and laparoscopically assisted arms was 75.3% and 75.8%, respectively. The 95% CI of the difference (open minus laparoscopically assisted surgery) ranged from –5% to 4%. The corresponding figures for overall survival were 83.5% and 82.2%, respectively, with the 95% CI of the difference ranging from –3% to 5%.

For various reasons, 6 patients had laparoscopic surgery despite randomization to the open arm and 5 patients had open surgery instead of laparoscopic surgery. The results of the analysis of disease-free survival and overall survival based on the received treatment did not differ from the results of the analysis based on the randomized procedure.

Cox proportional hazards regression model analyses for disease-free survival and overall survival stratified by trial, adjusting for sex, age, and tumor stage, revealed no differences between the treatments. The treatment effects did not significantly differ among the trials for disease-free survival ($P = .38$) or for overall survival ($P = .35$). The hazard ratios for the 4 trials separately and the pooled common hazard ratios are shown in (Figure 7) for disease-free survival and for overall survival.

Tumor recurrence was recorded in 234 patients (who underwent 121 open and 113 laparoscopic procedures). Of 121 recurrences in the open arm, 40 (33.1%) were local, 73 (60.3%) were distant metastases, and 8 (6.6%) were combined local and distant metastases; the corresponding figures in the laparoscopically assisted arm were 29 (25.7%), 74 (65.5%), and 10 (8.8%), respectively. These patterns did not significantly differ between the 2 treatment groups ($P = .43$, χ^2 test).

Disease-free survival and overall survival according to randomized treatment group by stage are shown in (Figure 8). Significant differences between the 2 treatments were not found in any stages for disease-free survival ($P = .92$, $P = .44$, and $P = .53$ for stages I, II, and III, respectively); the associated hazard ratios (laparoscopically assisted vs open surgery) were 1.03 (95% CI, 0.58-1.85), 1.14 (95% CI, 0.82-1.60), and 0.91 (95% CI, 0.68-1.22), respectively. Overall survival was similar between the randomized procedures for all stages as well ($P = .78$, $P = .09$, and $P = .52$ for stages I, II, and III, respectively); the associated hazard ratios were 1.10 (95% CI, 0.57-2.14), 1.40 (95% CI, 0.95-2.07), and 0.89 (95% CI, 0.61-1.28), respectively.

18. Figures and Tables

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 1. Mean or median duration of operation

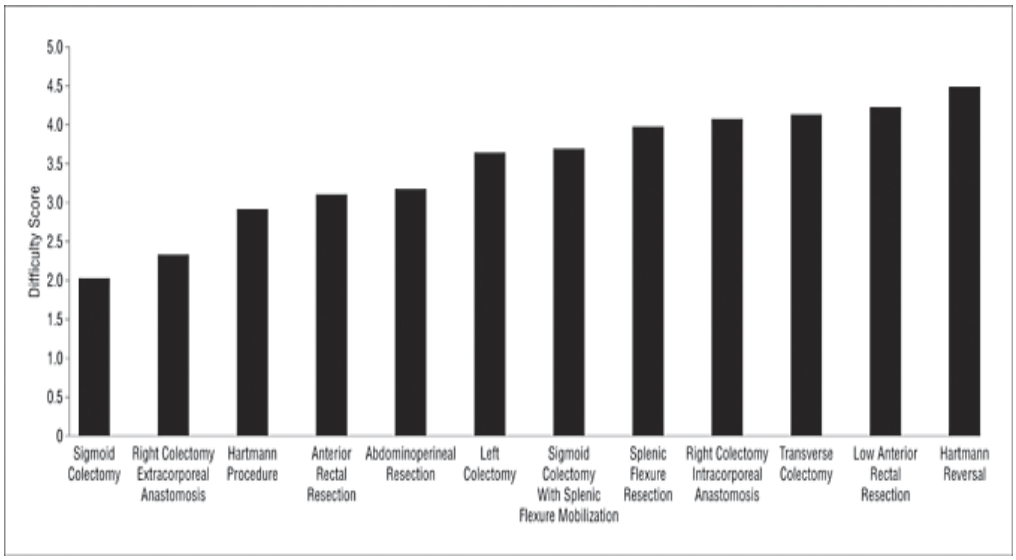

Figure 1. Overall difficulty score for each of the 12 rated procedures

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.

Table 2. Conversion rates by surgeon experience in performing laparoscopic colectomies

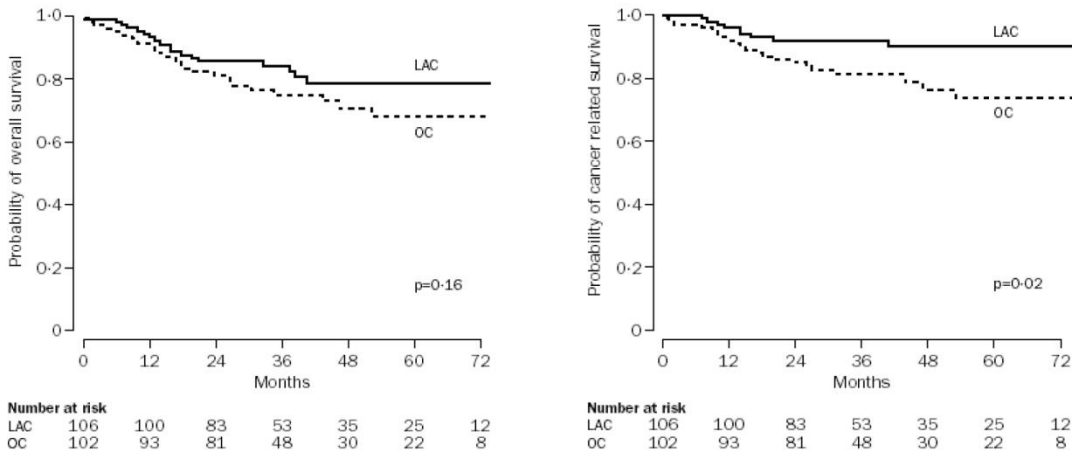

Figure 2. Overall survival-cancer related survival

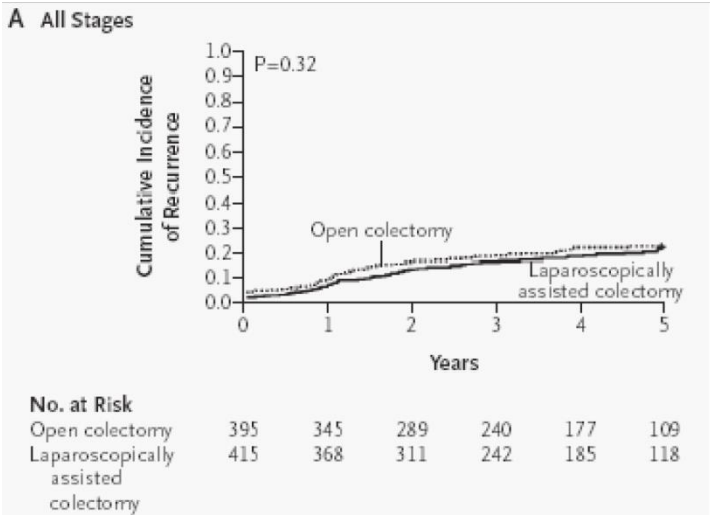

Figure 3. Reccurence-all stages

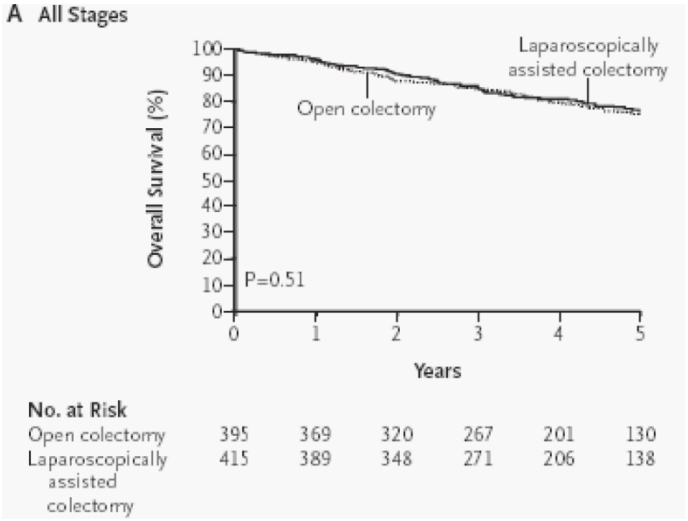

Figure 4. Survival-all stages

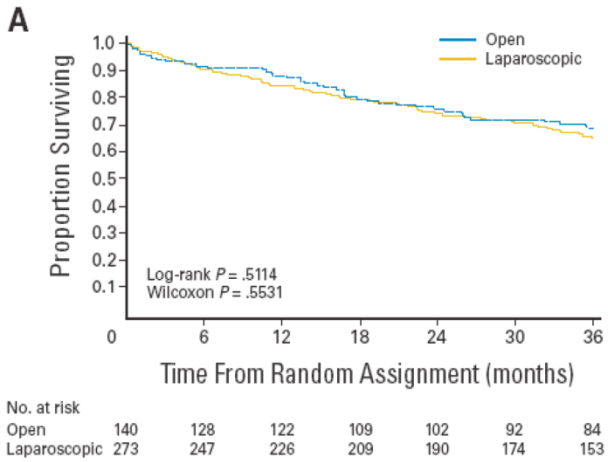

Figure 5. 3y OS colon cancer

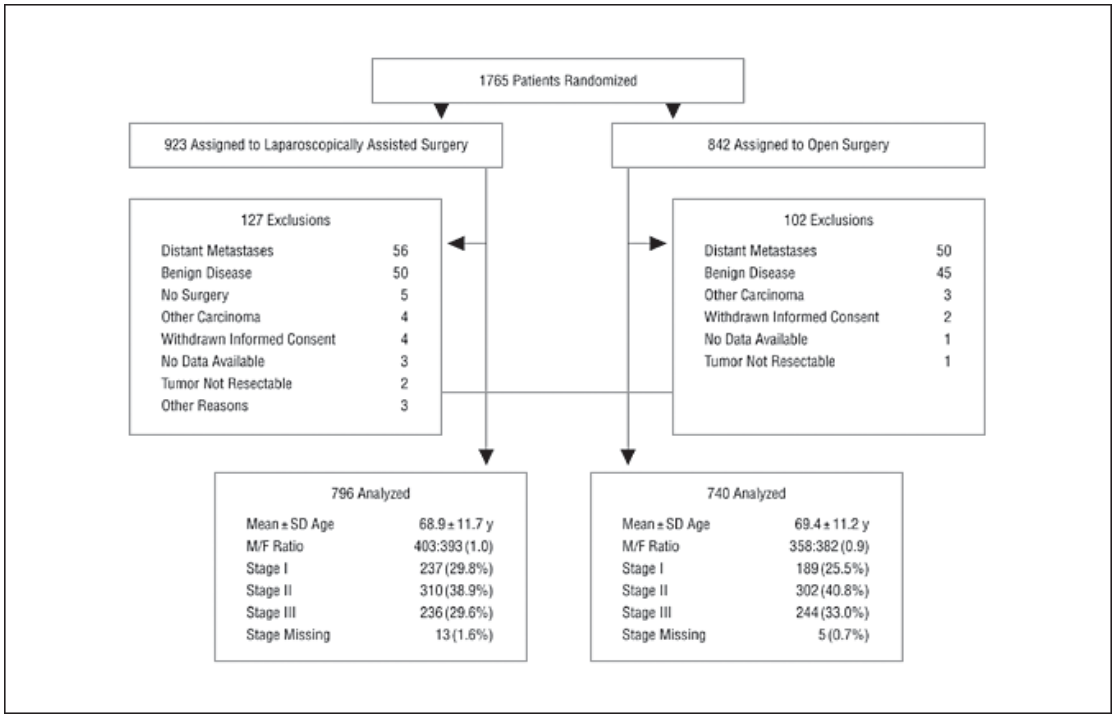

Figure 6. Patient characteristics.

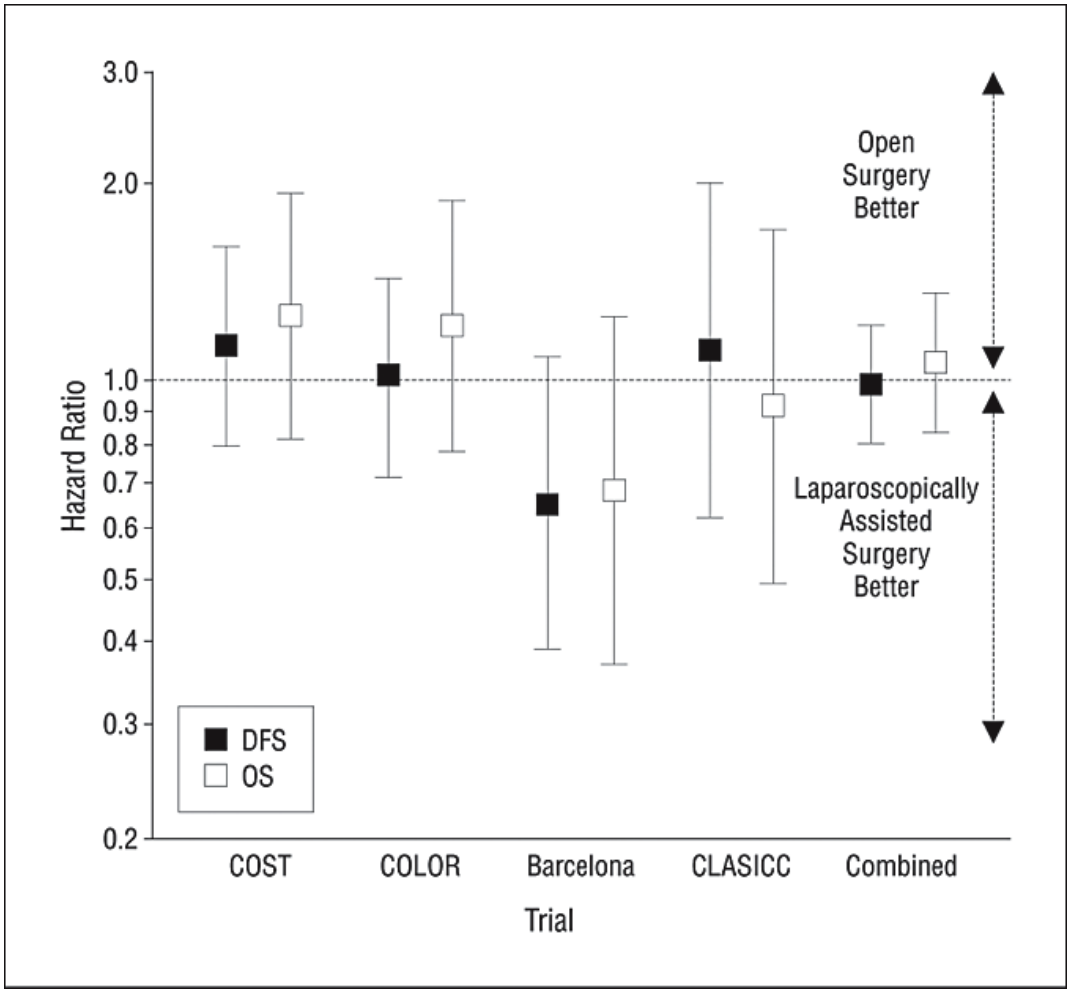

Figure 7. Hazard ratios (laparoscopically assisted surgery vs open surgery) with 95% confidence intervals regarding disease-free survival (DFS) and overall survival (OS) during the first 3 years after randomization according to study and for the 4 studies combined (adjusted for sex, age, and stage). Barcelona indicates Barcelona trial; CLASICC, Conventional vs Laparoscopic-Assisted Surgery in Patients With Colorectal Cancer trial; COLOR, Colon Cancer Laparoscopic or Open Resection trial; and COST, Clinical Outcomes of Surgical Therapy trial.

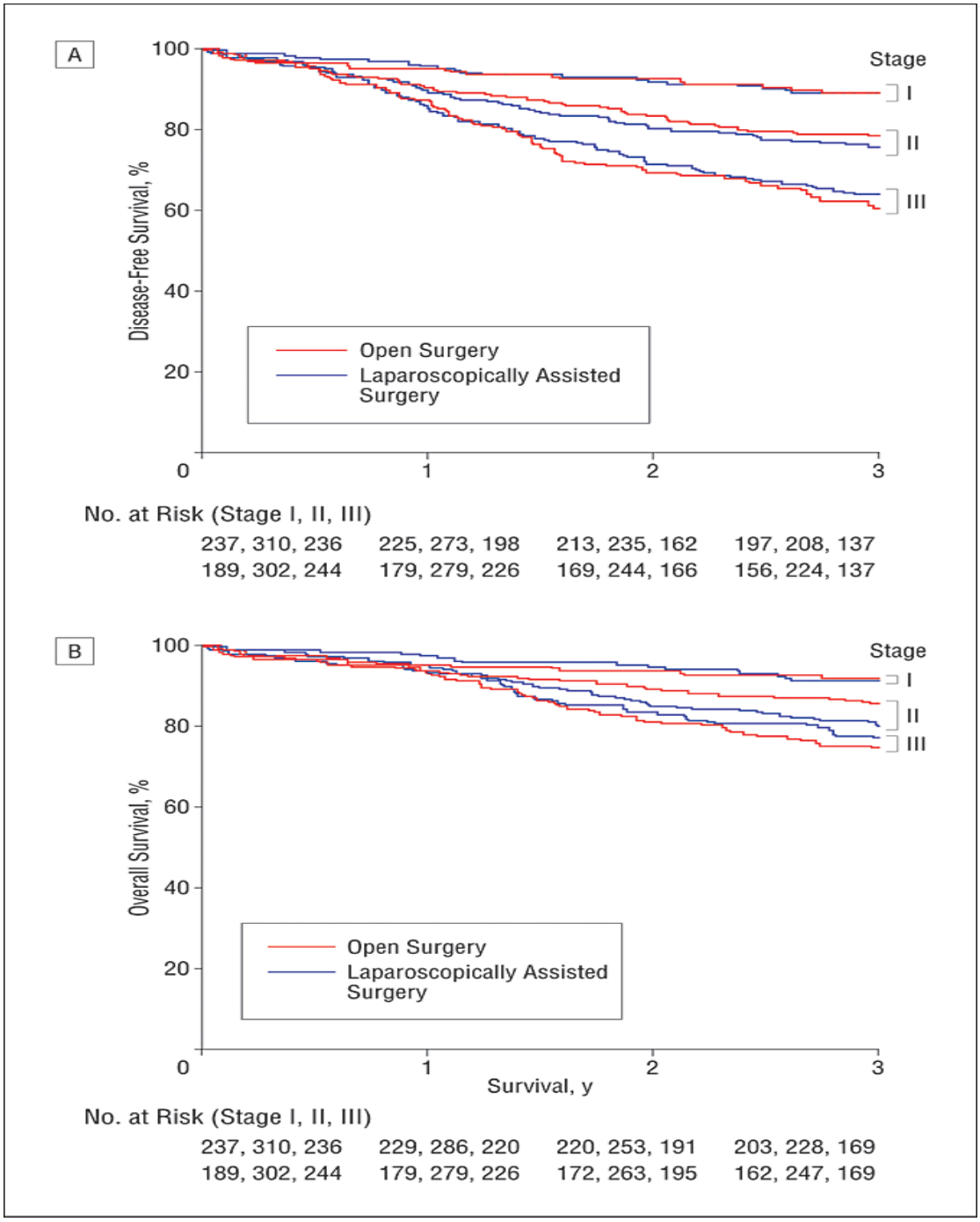

Figure 8. Disease-free survival (A) and overall survival (B) according to randomized procedure and stage. The numbers of patients at risk for each stage are shown at the bottom: the top row gives the numbers who underwent laparoscopically assisted surgery; the bottom row, open surgery.

19. Discussion

The role of laparoscopy in colon surgery is currently being debated. Theoretical advantages to laparoscopy include less intra-operative fluid loss and thus less postoperative fluid shifts, fewer adhesions leading to fewer postoperative bowel obstructions, and less immunosuppression, possibly resulting in improved survival. Bohm et al.,[38] demonstrated that the normal myoelectric activity of the stomach, small bowel, and colon returned faster in dogs that underwent laparoscopic right colon resections than in those receiving a traditional open procedure. Other factors that may contribute to a faster return of bowel function in laparoscopic patients are decreased narcotic analgesic usage and less intraoperative manipulation of the bowel. One disadvantage has been the increased duration of the operation.

The feasibility and safety of laparoscopic colorectal resection have been repeatedly reported. The rate of conversion to open surgery is low when strict eligibility criteria are applied and the surgical team is well trained. [39-41] The highest conversion rates were reported in series resulting from early experiences. [42,43]

Some concerns remain about the oncologic adequacy of laparoscopy, although the data published so far are promising. No difference was found in the exfoliation of cancer cells in the peritoneal lavage before and after colon resection by comparing laparoscopic and open surgery. [44] The number of lymph nodes collected was similar for both techniques, [45,46] probably because the same oncologic principles for lymph vascular pedicle division and the extent of colonic resection were applied. With the exception of the earliest series, [47] the port-site recurrence rate is not different from wound recurrence rate reported following open colectomy. Furthermore, the few studies focusing on cancer recurrence and patient survival did not report a substantial difference between laparoscopic and open surgery. [48]

Laparoscopic colorectal surgery seems to be associated with less tissue injury than open surgery. Thus, some hypothetical benefits can be expected, such as better preservation of systemic immune function, a less pronounced postoperative inflammatory response, reduced postoperative pain, and faster recovery of intestinal motility and function. This might translate into an improved outcome. In contrast, the potential disadvantages of laparoscopic surgery are the longer operative time and the higher charges for surgical devices and instruments compared to open surgery.

Moreover, two studies reported that laparoscopic surgery caused a higher mental strain for surgeons. [49]

It is difficult to draw any firm conclusions as to the advantage of laparoscopic surgery on clinically relevant variables because the results of published trials are often conflicting. [46,50] This may be due to several reasons: few and underpowered randomized clinical trials have been performed, intention-to-treat analysis of results has been occasionally violated, no a priori definition of complications has been given (particularly important in no blinded studies), and criteria for patient selection often differ. To overcome these potential biases, the power of the study was calculated a priori based on the complication rate of our previous trials,[41] five separate randomization lists according to the site of the lesion were generated to obtain a balanced distribution of different surgical procedures, strict inclusion and exclusion criteria were used, postoperative complications were rigorously defined a priori, [51] and the analysis of results was carried out on an intention-to-treat basis.

The analysis of the operative variables confirmed that the laparoscopic operation was longer than open surgery, according to previous studies. [41,46] Our results showed that blood loss was significantly lower in the laparoscopic group than in the open group. This finding is consistent with the results by Psaila et al, while other authors found no difference in the operative blood loss by comparing the two techniques. [46,52] However, the lower blood loss observed in the laparoscopic group was not associated with a significant reduction in the homologous transfusion rate.

In the present trial, the laparoscopic group had a significantly lower postoperative complication rate compared to the open group. This is consistent with data recently reported by Milsom et al, who randomized 60 patients undergoing ileocolic resection for refractory Crohn's disease, and by Liang et al [53] in a series of patients undergoing sigmoid resection for complex polyps. In particular, the laparoscopic technique significantly reduced the incidence of wound infections, possibly because of minimal wound contamination, the shorter incision, and less manipulation of the intestine. The wound infection rate found in the present series is similar to the pooled rate calculated by Chapman et al in a systematic review of trials on laparoscopic colorectal resection. The relatively high morbidity rate registered in the open group suggests some caution in the generalizability of the present data. However, the postoperative infection rate in the open group was consistent with

intent-to-treat analysis from our previous trials. [54] A strict 30-day follow-up is a key point to obtain reliable data on the incidence of postoperative infections. [55] In fact, in the present series about 30% of postoperative infections (most of them were surgical wound infections) occurred after discharge. The rate of anastomotic leak and reoperation was not significantly different between groups. The incidence of clinically and/or radiologically evident anastomotic leak in the open group was comparable with our previous reports. [54] In both groups, anastomotic leak was the more frequent cause of reoperation. This reflects our policy in patients with clinically evident anastomotic dehiscence, which consists of both lavage of the peritoneal cavity and construction of a proximal ostomy.

Previous studies comparing laparoscopic and open colorectal surgery found a significant shorter hospital stay following laparoscopy. [46,52] In the present series, the lower postoperative complication rate combined with the earlier recovery of both bowel function and oral feeding may represent important determinants for the reduced length of hospital stay in the laparoscopic group. Other factors that could explain the shorter hospital stay following laparoscopy are the lower postoperative pain/consumption of analgesic drugs [41] and the earlier recovery of self-care score and full ambulation ability. In Italy, the hospital stay is usually longer than in the United States. This is due to the lack of outpatient guesthouses; thus, the patients completed postoperative recovery in the hospital before being discharged. In our study, patients who underwent laparoscopic surgery recovered full physical and social activity about 30 days earlier than the patients in the open group.

According to Liang et al, [53] this study showed that laparoscopy was more expensive than open surgery, although the shorter hospital stay nearly compensated for the additional costs of surgical instruments and devices and the longer operative time. To better evaluate the cost/benefit balance of laparoscopy, a precise quantification should be made of both the healthcare resources consumed by postoperative complications and the impact of the social cost of the faster recovery of full physical and social activity.

The real advantage of laparoscopic colorectal operation on the immune and inflammatory responses is still debated. [41] The conflicting results of previous trials are probably due to the different immune parameters investigated and the different techniques used to measure postoperative immune response. In the present study, both

polyclonal stimulation and antigen-specific stimulation were used to evaluate the immune status of patients. PHA stimulates the proliferation of the whole T-cell population, while *C. albicans* selectively stimulates the Th1 inflammatory type of CD4+ T cells, which secrete IFN-gamma and TNF-alfa and migrate selectively from the circulation into inflamed tissue following the release of soluble mediators of inflammation. PHA stimulation shows that the suppressive effect of open surgery on the whole T-cell population was more evident 15 days after operation, whereas no suppressive effect was found in the laparoscopic group. The selective analysis of Th1 proliferation showed a significant impairment in both groups early after surgery. This is likely due to the migration of Th1 cells from the circulation into the injured tissue. To explain the quicker recovery of Th1 cellsβ€™ proliferative ability in the laparoscopic group, it may be hypothesized that laparoscopy induced a less pronounced local inflammation than open surgery. This might result in a faster return of Th1 cells from tissues into the blood, with consequent recovery of their proliferation ability on postoperative day 15. This hypothesis is consistent with the lower levels of proinflammatory mediators observed after laparoscopy compared to open surgery. [41]

High-pressure pneumoperitoneum has been shown to impair splachnic perfusion and oxygenation in animal models. [56] Potential determinants of such effect are hypercapnia and its systemic effects on haemodynamics, reduced venous return, elevated diaphragm, and increased thoracic pressure. In humans, only one trial has investigated the impact of laparoscopy on bowel microperfusion by the laser Doppler technique. The authors found a 44% reduction in the colonic microperfusion during laparoscopic surgery, but it was promptly reversed by the interruption of pneumoperitoneum. [57] No data have been published so far about the effect of laparoscopy on gut oxygen tension in humans. In the present study, a higher bowel oxygen tension was found at the beginning of surgery before any gut manipulation, and during the entire surgical procedure in the laparoscopic group. Many factors could explain this finding, such as the less traumatic abdominal incision, less traction on the mesentery, and the relative low-pressure pneumoperitoneum used. The clinical impact of these data remains unknown. Nevertheless, it may be speculated that the higher oxygen tension during laparoscopic surgery plays an important role in

improving the systemic host response, early recovery of gut function, and local wound repair.

In conclusion, the laparoscopic technique resulted in a reduction of both the overall morbidity rate and the length of hospital stay, and in a faster recovery of physical and social activity. The surgery-related impairment of lymphocyte proliferation and gut oxygen tension was less pronounced in the laparoscopic than in the open group.

20. Conclusion

The first series of laparoscopic colonic resections in the United States were reported in 1991. As more evidence from randomized trials demonstrated the efficacy and safety of the laparoscopic approach, surgeons were pressured to offer minimally invasive procedures to patients with colorectal pathology. In experienced hands, laparoscopic surgery has been shown to offer patients real advantages in decreased postoperative pain, shorter hospitalization, better cosmesis, and a quicker return to normal activity. Therefore, this procedure has been embraced by many clinicians as a reasonable treatment option for benign colonic disorders or as a palliative procedure in those unfortunate individuals with distant metastatic cancer. On the contrary, laparoscopic surgery was taken under consideration when the candidates for laparoscopic surgery were patients with localized cancer.

One concern about the laparoscopic approach for treatment of colon cancer is whether laparoscopic techniques can achieve true "oncologic" resection (i.e., wide margins and intact resection of areas of lymph node drainage) of the colon. Studies of animal and cadaver models measured the length of divided major arterial supply (i.e., inferior mesenteric artery) and the amount of lymph nodes remaining after resection of the colon to show that laparoscopic techniques could adhere to principles of cancer surgery. The adequacy of lymphadenectomy has been addressed by several studies, which consistently showed that the number of lymph nodes resected laparoscopically was similar to the number retrieved in open colectomy for cancer.

21. Abstract

Objective

To compare the safety and efficacy of laparoscopic resection of colorectal diseases with open colectomy.

Methods

Two search strategies were devised to retrieve literature from the Medline, Current Contents, Embase, and Cochrane Library databases until December 2010. 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. The papers were tabulated and critically appraised in terms of methodology and design, outcomes, and the possible influence of bias, confounding, and chance.

Results

Although laparoscopic resection of colorectal diseases was more expensive and time-consuming, the procedure offered earlier recovery from surgery and reduced pain. There was no significant difference between the conventional open technique and the laparoscopic one for colon resection for cancer, concerning the primary and secondary outcomes.

Conclusions

Laparoscopic resection for colon diseases has been prooved as a safe and efficient method. It has statistically and clinically significant advantages over open colectomies with respect to the length of hospital stay, earlier recovery of bowel function , need for fewer analgesics. Morbidity and mortality do not differ between two techniques.

22.Περίληψη

Εισαγωγή

Να συγκρίνει την ασφάλεια και την επιτευξιμότητα της λαπαροσκοπικής εκτομής των βλαβών του παχέος εντέρου με την ανοικτή μέθοδο.

Υλικό – Μέθοδοι

Δύο κύριες πηγές χρησιμοποιήθηκαν για την ανεύρεση της βιβλιογραφίας από το Medline, Current Contents, Embase και από τη βάση δεδομένων Cochrane Library μέχρι το Δεκέμβριο του 2010. Για να συμπεριλήφθούν τα άρθρα θα έπρεπε να χρησιμοποιούν ένα προκαθορισμένο πρωτόκολλο, ανεξάρτητη εκτίμηση από δύο ερευνητές και ένα τελικό ξεκάθαρο αποτέλεσμα. Τα άρθρα επιλέγησαν στην αγγλική γλώσσα. Αποδεκτές εργασίες περιλαμβάνουν τυχαιοποιημένες μελέτες, κλινικές μελέτες, σειρές αναφοράς ή περιστατικά αναφοράς. Τα άρθρα συνοψίστηκαν, εκτιμήθηκαν και βγήκαν ασφαλή συμπεράσματα .

Αποτελέσματα

Παρ'όλο που η λαπαροσκοπική εκτομή των παθήσεων του παχέος εντέρου είναι πιο ακριβή και πιο χρονοβόρα, η μέθοδος προσφέρει γρηγορότερη ανάρρωση και λιγότερο μετεγχειρητικό πόνο. Δεν παρατηρείται στατιστικά σημαντική διαφορά μεταξύ της ανοιχτής και της λαπαροσκοπικής μεθόδου, όσον αφορά τις άμεσες και τις απώτερες επιπλοκές.

Συμπεράσματα

Η λαπαροσκοπική εκτομή των παθήσεων του παχέος εντέρου έχει αποδειχθεί ως ασφαλής και αποτελεσματική μέθοδος. Προσφέρει στατιστικά και κλινικά σημαντικά πλεονεκτήματα σε σύγκριση με τις ανοικτές επεμβάσεις, ως προς το χρόνο νοσηλείας, την ταχύτερη λειτουργία του γαστρεντερικού συστήματος και την αναλγησία. Τα ποσοστά νοσηρότητας και η θνητότητας δεν διαφέρουν μεταξύ των δύο μεθόδων.

23. References

1. Canadian Cancer Society. Media backgrounder: Colorectal Cancer Statistics. Toronto: the Society; 2002. Electronic Citation; http://www.cancer.ca.
2. Lord SA, Larach SW, Ferrara A, et al. Laparoscopic resections for colorectal carcinoma. A three-year experience. *Dis Colon Rectum* 1996;39:148-54..
3. Fleshman JW, Nelson H, Peters WR, et al. Early results of laparoscopic surgery for colorectal cancer. Retrospective analysis of 372 patients treated by Clinical Outcomes of Surgical Therapy (COST) Study Group. *Dis Colon Rectum* 1996;39:S53-8.
4. Lacy AM, Garcva-Valdecasas JC, Delgado S, et al. Laparoscopy assisted colectomy versus open colectomy for treatment of nonmetastatic colon cancer: a randomised trial. *Lancet* 2002;359:2224-9.
5. Jayne DG, Guillou PJ, Thorpe H, et al. Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC trial group. *J Clin Oncol* 2007;25:3061-8.
6. Jacobs M, Verdeja JC, Goldstein HS. Minimally invasive colon resection (laparoscopic colectomy). *Surg Laparosc Endosc* 1991; 1: 144 50.
7. Joo JS, Amarnath L, Wexner SD. Is laparoscopic resection of colorectal polyps beneficial? *Surg Endosc* 1998; 12: 1341–4.
8. Liberman MA, Phillips FH, Carroll BJ, Fallas M, Rosenthal R. Laparoscopic colectomy vs traditional colectomy for diverticulitis. *Surg Endosc* 1996; 10: 15–8.
9. IHS Health Group (Medical Data International).U.S. Surgical Procedure Volumes*:* 2001. Englewood, CO: IHS Health Group (Medical Data International), 2001.
10. The Clinical Outcomes of Surgical Therapy Study Group. A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med. 2004;350:2050-2059.
11. Leung K, Kwok S, Lam S, et al. Laparoscopic resection of rectosigmoid carcinoma: prospective randomised trial. Lancet. 2004;363:1187-1192.

12. Lacy A, Garcia-Valdecasas J, Delgado S, et al. Laparoscopic-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. Lancet. 2002;359:2224-2229.
13. Franks PJ, Bosanquet N, Thorpe H, et al. Short-term costs of conventional vs laparoscopic assisted surgery in patients with colorectal cancer (MRC CLASICC trial). Br J Cancer. 2006;95:6-12.
14. Janson M, Bjorholt I, Carlsson P, et al. Randomized clinical trial of the costs of open and laparoscopic surgery for colonic cancer. Br J Surg. 2004;91:409-417.
15. Barker K, Graham NG, Mason MC, De Dombal FT, Goligher JC. The relative significance of preoperative oral antibiotics, mechanical bowel preparation, and preoperative peritoneal contamination in the avoidance of sepsis after radical surgery for ulcerative colitis and Crohn's disease of the large bowel. Br J Surg. 1971;58:270-273.
16. Zmora O, Mahajna A, Bar-Zakai B, et al. Colon and rectal surgery without mechanical bowel preparation: a randomized prospective trial. Ann Surg. 2003;237:363-367.
17. *Bruce V. Mac Fadyen, Jr., MD, et al.,Editors. Laparoscopic Surgery of the Abdomen.2003;s335-s352*
18. Jean-Louis Dulucq.Tips and Techniques in Laparoscopic Surgery 2003;s119-s153
19. Shah PR, Joseph A, Haray PN. Laparoscopic colorectal surggery: learning curve and training implications. *Postgrad Med J* 2005;81(958):537–40.
20. Bennett CL, Stryker SJ, Ferreira MR, et al. The learning curve for laparoscopic colorectal surgery. Preliminary results from a prosspective analysis of 1194 laparoscopic-assisted colectomies. *Arch Surg* 1997;132(1):41–4.
21. Agachan F, Joo JS, Weiss EG, Wexner SD. Intraoperative laparosscopic complications. Are we getting better? *Dis Colon Rectum* 1996;39(10 Suppl):S14–19.
22. Schwandner O, Schiedeck TH, Bruch H. The role of conversion in laparoscopic colorectal surgery: do predictive factors exist? *SurgEndosc* 1999;13(2):151–6.

23. Sim R, Milsom JW. Laparoscopic colectomy for malignancy. *SeminLaparosc Surg* 2000;7(2):101–17.
24. Turnbull RB Jr, Kyle K, Watson FR, Spratt J. Cancer of the colon: the influence of the no-touch isolation technique on survival rates. *Ann Surg.* 1967;166:420-427.
25. Fitzgerald SD, Andrus CH, Baudendistel LJ, Dahms TE, Kaminski DL. Hypercarbia during carbon dioxide pneumoperitoneum. *Am J Surg.* 1992;163:186-190.
26. Wahba RWM, Mamazza J. Ventilatory requirements during laparoscopic cholecystectomy. *Can J Anaesth.* 1993;40:206-210.
27. 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.
28. Delgado F, Bolufer JM, Grau E, et al. Laparoscopic colorectal cancer resection, initial follow-up results. Surg Laparosc Endosc 1999; 9: 91-98.
29. 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.
30. Mutch MG Laparoscopic colectomy in the elderly: when is too old?Clin Colon Rectal Surg. 2006 Feb;19(1):33-9
31. Lacy AM, García-Valdecasas JC, Delgado S, Castells A, Taurá P, Piqué JM, Visa J. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. Lancet. 2002 Jun 29;359(9325):2224-9.
32. Stucky CC, Pockaj BA, Novotny PJ, Sloan JA, Sargent DJ, O'Connell MJ, Beart RW, Skibber JM, Nelson H, Weeks JC. Long-Term Follow-Up and Individual Item Analysis of Quality of Life Assessments Related to Laparoscopic-Assisted Colectomy in the COST Trial 93-46-53 (INT 0146). Ann Surg Oncol. 2011 Mar 31.
33. Leung KL, Kwok SP, Lam SC, Lee JF, Yiu RY, Ng SS, Lai PB, Lau WY. Laparoscopic resection of rectosigmoid carcinoma: prospective randomised trial. Lancet. 2004 Apr 10;363(9416):1187-92.
34. Jayne DG, Guillou PJ, Thorpe H, Quirke P, Copeland J, Smith AM, Heath RM, Brown JM; UK MRC CLASICC Trial Group. Randomized trial of

laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC Trial Group. J Clin Oncol. 2007 Jul 20;25(21):3061-8.

35. Veldkamp R, Kuhry E, Hop WC, Jeekel J, Kazemier G, Bonjer HJ, Haglind E, Påhlman L, Cuesta MA, Msika S, Morino M, Lacy AM; COlon cancer Laparoscopic or Open Resection Study Group (COLOR). Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. Lancet Oncol. 2005 Jul;6(7):477-84.
36. Hewett PJ, Allardyce RA, Bagshaw PF, Frampton CM, Frizelle FA, Rieger NA, Smith JS, Solomon MJ, Stephens JH, Stevenson AR. Short-term outcomes of the Australasian randomized clinical study comparing laparoscopic and conventional open surgical treatments for colon cancer: the ALCCaS trial. Ann Surg. 2008 Nov;248(5):728-38.
37. Fleming ID, Cooper JS, Henson DE; et al. *AJCC Cancer Staging Manual.* 5th ed. New York, NY: Wiley-Liss; 1997.
38. Stephen K. Muckleroy, MD, Erick R. Ratzer, MD, and Michael E. Fenoglio, MD Laparoscopic Colon Surgery for Benign Disease: A Comparison to Open Surgery. JSLS. 1999 Jan–Mar; 3(1): 33–37.
39. Wexner SD, Reissman P, Pfeifer J, et al. Laparoscopic colorectal surgery. Analysis of 140 cases. Surg Endosc 1996; 10: 133-136.
40. Bruch HP, Schiedeck TH, Schwandner O. Laparoscopic colorectal surgery. A five-year experience. Dig Surg 1999; 16: 45-54.
41. Braga M, Vignali A, Zuliani W, et al. Metabolic and functional results after laparoscopic colorectal surgery. A randomized controlled trial. Dis Colon Rectum 2002; 45: 1070-1077.
42. Molenaar CB, Bijnen AB, de Ruiter P. Indications for laparoscopic colorectal surgery: results from the medical centre Alkmaar, The Netherlands. Surg Endosc 1998; 12: 42-45.
43. Delgado F, Bolufer JM, Grau E, et al. Laparoscopic colorectal cancer resection, initial follow-up results. Surg Laparosc Endosc 1999; 9: 91-98.
44. 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.

45. 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
46. Lacy AM, Carcia-Valdecasas JC, PiquΓ¨; MJ, et al. Short-term outcome analysis of a randomised study comparing laparoscopic vs open colectomy for colon cancer. Surg Endosc 1995; 9: 1101-1105.
47. Nduka CC, Monson JR, Menzies GN, et al. Abdominal wall metastases following laparoscopy. Br J Surg 1994; 81: 648-652.
48. 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.
49. Bohm B, Rotting N, Schwenk W, et al. A prospective randomized trial on heart rate variability of the surgical team during laparoscopic and conventional sigmoid resection. Arch Surg 2001; 136: 305-310.
50. Tate JJT, Kwok S, Dawson JW, et al. Prospective comparison of laparoscopic and conventional anterior resection. Br J Surg 1993; 80: 1396-1398.
51. Bozzetti F, Braga M, Gianotti L, et al. Postoperative enteral versus parenteral nutrition in malnourished patients with gastrointestinal cancer: a randomised multicentre trial. Lancet 2001; 358: 1487-1492.
52. 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.
53. Liang JT, Shieh MJ, Chen CN, et al. Prospective evaluation of laparoscopy-assisted colectomy versus laparotomy with resection for management of complex polyps of the sigmoid colon. World J Surg 2002; 26: 377-383.
54. Braga M, Gianotti L, Vignali A, Di Carlo V. Preoperative oral arginine and n-3 fatty acid supplementation improves the immunometabolic host response and outcome after colorectal resection for cancer. Surgery (in press).
55. Keeling NJ, Morgan MWE. Inpatient and postdischarge wound infections in general surgery. Ann R Coll Surg Engl 1995; 77: 245-247.
56. Schafer M, Krahenbuhl L. Effect of laparoscopy on intra-abdominal blood flow. Surgery 2001; 129: 385-389.
57. Schilling MK, Redaelli C, Krahenbuhl L, et al. Splanchnic microcirculation changes during CO_2 laparoscopy. J Am Coll Surg 1997; 184: 378-382.