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SURGICAL ENDOSCOPY
and Other Interventional Techniques

Laparoscopic resection of colon cancer

Consensus of the European Association of Endoscopic Surgery (E.A.E.S.)

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Abstract
Background: The European Association of Endoscopic Surgery (EAES) initiated a consensus development conference on the laparoscopic resection of colon cancer during the annual congress in Lisbon, Portugal, in June 2002.
Methods: A systematic review of the current literature was combined with the opinions, of experts in the field of colon cancer surgery to formulate evidence-based statements and recommendations on the laparoscopic resection of colon cancer.
Results: Advanced age, obesity, and previous abdominal operations are not considered absolute contraindications for laparoscopic colon cancer surgery. The most common cause for conversion is the presence of bulky or invasive tumors. Laparoscopic operation takes longer to perform than the open counterpart, but the outcome is similar in terms of specimen size and pathological examination. Immediate postoperative morbidity and mortality are comparable for laparoscopic and open colonic cancer surgery. The laparoscopically operated patients had less postoperative pain, better-preserved pulmonary function, earlier restoration of gastrointestinal function, and an earlier discharge from the hospital. The postoperative stress response is lower after laparoscopic colectomy. The incidence of port site metastases is $<1\%$. Survival after laparoscopic resection of colon cancer appears to be at least equal to survival after open resection. The costs of laparoscopic surgery for colon cancer are higher than those for open surgery.
Conclusion: Laparoscopic resection of colon cancer is a safe and feasible procedure that improves short-term outcome. Results regarding the long-term survival of patients enrolled in large multicenter trials will determine its role in general surgery.

Key words: Laparoscopic resection — Colon cancer — Contraindications — Conversion — Morbidity and mortality — Outcomes — Stress response — Port site metastasis — Costs

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Table 1. A method for grading recommendations according to scientific evidence

Grade of recommendation	Level of evidence	Possible study designs for the evaluation of therapeutic interventions
A	1a	Systematic review (with homogeneity) of RCT
	1b	Individual RCT (with narrow confidence interval)
	1c	All or none case series
B	2a	Systematic review (with homogeneity) of cohort studies
	2b	Individual cohort study (including low-quality RCT)
	2c	"Outcomes" research
	3a	Systematic review (with homogeneity) of case-control studies
	3b	Individual case-control study
C	4	Case series (and poor-quality cohort and case-control studies)
D	5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles," animal studies

RCT, randomized controlled trial(s)
From Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB (2000) Evidence-based medicine: how to practice and teach EBM. 2nd ed. Churchill Livingstone, London

Laparoscopic surgery for colon cancer remains controversial. Because of early reports of port site metastases, many surgeons refrained from following the laparoscopic approach to colon cancer, despite evidence from experimental tumor biology studies that have indicated clear oncological benefit of laparoscopic surgery.

Multi-center clinical trials randomizing patients with colon cancer to either laparoscopic or open resection were initiated in the mid 1990s to assess the oncological safety of laparoscopic surgery. Because a minimum follow-up period of 3 years is required to establish cancer-free survival rates, none of these ongoing randomized trials has yet accumulated sufficient data that would enable reliable and definitive assessment of laparoscopic colectomy for cancer.

This consensus conference (CC) addresses only colon cancer. Rectal cancer has been excluded because the available experience with laparoscopic surgery for rectal cancer is limited and because the treatment of rectal cancer differs from that of colon cancer in many respects.

The objectives of the consensus conference were:

1. To establish the preferred diagnostic procedures, selection of patients, and surgical technique of laparoscopic resection of colon cancer.
2. To assess the radicality, morbidity, hospital stay, costs, and recovery from laparoscopic resection of colon cancer.
3. To define standards and optimal practice in laparoscopic colon cancer surgery and provide recommendations/statements that reflect what is known and what constitutes good practice.

Methods

The consensus recommendations and statements are based on a systematic review of the literature and a consensus development conference (CDC) held in Lisbon, Portugal, during the 2002 congress of the EAES. They are summarized in the Appendix.

A panel of experts in both open and laparoscopic surgery were recruited for the CDC and to assist in the formulation of the consensus. Each expert had to complete independently a detailed questionnaire on laparoscopic resection of colon cancer, participate in the CDC, and review the consensus document. A reference list with accompanying abstracts was provided to the experts, who were asked to provide details of published articles not included in the bibliography that had been sent to them. The questionnaire covered key aspects of laparoscopic resections of colon cancer. The personal experience of the experts, their opinions, or references drawn from the literature search formed the basis for completion of the questionnaire. In parallel, the questions were also addressed by performing a systematic review of the relevant literature.

The systematic review was based on a comprehensive literature search of Medline, Embase, and the Cochrane Library. The following query was used to identify relevant articles: (colectom* OR hemicolectom* OR colon resection) AND (laparoscop* OR endoscop* OR minimal* invasive) AND (colorect* OR colon OR intestine, large) AND (malignanc* OR cancer OR adenocarcinoma* OR carcinoma* OR tumor* OR tumour* OR metastas* OR neoplas*) NOT (FAP OR familial adenomatous polyposis OR HNPCC OR hereditary nonpolyposis OR inflammatory bowel disease OR ulcerative colitis OR Crohn* OR diverticulitis). Only the terms –colon cancer– and –laparoscopy– were used in the Cochrane search because the previous query was too restricted and hence inappropriate for the Cochrane database. Relevant articles were first selected by title; their relevance to the objectives of the consensus conference was then confirmed by reading the corresponding abstracts. Missing articles were identified by hand searches of the reference lists of the leading articles and from articles brought to the attention of the organizing group by the experts. The primary objective of the search was to identify all clinically relevant randomized controlled trials (RCT). However, other reports (e.g., using concurrent cohort, external, or historical control), population-based outcomes studies, case series, and case reports were also included. All articles were categorized by two reviewers (R. Veldkamp and H. J. Bonjer) according to the quality of data and evidence they provided (Table 1).

The systematic review of the literature provided evidence on extent of the resection, morbidity, mortality, hospital stay, recovery, and costs of laparoscopic colon cancer surgery. Regrettably, the level of evidence of articles on surgical technique is low according to the Cochrane classification, indicating that surgical techniques are difficult to evaluate scientifically because many important aspects–e.g., multi-limb coordination, dexterity, tactile and visual appreciation of anatomical structures, and surgical experience–cannot be measured objectively.

Analysis of the completed questionnaires and the information culled from the systematic review as outlined above formed the basis for the formulation of the draft consensus document, which was reviewed by the experts 3 weeks before the CDC in Lisbon, when all the panelists met for the first time on 2 June 2002. All statements, recommendations, and clinical implications with grades of recommendation were discussed during a 6-h session in terms of the prevailing internal (expert opinion) and external evidence. The following day, the consensus document with its clinical implications was presented to the conference audience by all panelists for public discussion. All suggestions from the audience were discussed, and the consensus document was modified where appropriate. In the following months, the consensus proceedings were published online on the Internet page of the

EAES. All members of the EAES were invited to comment on the consensus proceedings on a forum Web page. Sixteen surgeons commented on the consensus proceedings through the Internet forum. The modified final consensus document was approved by all the panelists before publication.

Preoperative evaluation and selection of patients

Preoperative imaging

In current practice, the same preoperative workup is done prior to both laparoscopic and conventional colectomies. Metastatic spread of colonic cancer is commonly investigated by ultrasonography of the liver and plain radiography of the chest. Colonoscopic biopsy specimens from the tumor are taken in most patients to confirm the presence of cancer. However, colonoscopy does not accurately localize the lesion [1]. Abdominal CT imaging to assess the size of the tumor and possible invasion of adjacent tissues is performed selectively at some European centers and more extensively in the United States.

The size of the colonic tumor is one of the important criteria for establishing the suitability of laparoscopic resection. The atraumatic and protected removal of a tumor that has been mobilized laparoscopically requires an incision of the abdominal wall. The laparoscopic approach is not indicated when the size of this incision for extraction approximates the size of a conventional laparotomy. Hence, preoperative knowledge about the size of the tumor improves selection and reduces the need for conversion.

Barium enema studies provide reliable data on the localization of colon cancer but do not show invasion of the tumor in the colonic wall or surrounding structures [2]. Conventional CT of the colon can also provide information about the localization of the tumor. In the near future, more advanced radiologic techniques, such as virtual colonoscopy, may be able to assess the site of the tumor more precisely [3, 4].

Cancerous invasion of organs adjacent to the colon can be detected by CT. However, the accuracy of preoperative staging of colon cancer by CT varies from 40% to 77% [3] because of the limited soft tissue contrast of CT, which impairs assessment of mural invasion by the tumor. The importance of tumor size and infiltration of surrounding structures is documented by a review of the causes of conversion during laparoscopic colonic surgery which indicated that almost 40% of conversions were due to a bulky or adherent tumor (see Conversion rate).

Laparoscopy has the potential to assess tumor invasion of adjacent organs, but there are no published reports on the value of laparoscopic staging in the workup and selection of patients for open or laparoscopic resection of colon cancer as distinct from its established use in gastric, pancreatic, and esophageal tumors.

Recommendation 1: Preoperative imaging

Preoperative imaging studies of colon cancer to assess the size of the tumor, possible invasion of adjacent structures, and localization of the tumor are recommended in laparoscopic surgery for colon cancer (Level of evidence: 5, Recommendation: Grade D).

Contraindications

Age

The experts agreed that age is not a contraindication. This view is supported by a subanalysis of a case series by Delgado et al. [5], who reported significantly lower morbidity after laparoscopic resection compared to open colectomy in patients >70 years old. Schwandner et al. [6] performed a subanalysis of 298 patients undergoing laparoscopic or laparoscopic-assisted colorectal procedures. There were no statistically significant differences among the younger, middle aged, and older patients in terms of conversion rate (3.1% vs 9.4% vs 7.4%, respectively), major complications (4.6% vs 10.1% vs 9.5%, respectively), and minor complications (12.3% vs 15.2% vs 12.6%, respectively). However, duration of surgery, stay in the intensive care unit, and postoperative hospitalization were significantly longer in patients older than 70 years ($p < 0.05$).

Complications reported in case series involving elderly patients after laparoscopic cholecystectomy seem to compare favorably with open cholecystectomy studies [7, 8].

Statement 2: Contraindications: age

Age only is not a contraindication for laparoscopic resection of colon cancer (Level of evidence: 2b).

Cardiopulmonary condition

Cardiopulmonary consequences of the pneumoperitoneum were thoroughly reviewed in the EAES consensus statement of 2002 [9]. Relevant parts of this consensus have been enclosed in the current consensus. Decreased Cardiopulmonary function is not regarded a contraindication to laparoscopic resection of colon cancer.

Cardiovascular effects of pneumoperitoneum occur most often during its induction, and this should be considered when the initial pressure is raised for the introduction of access devices. In ASA I–II patients, the hemodynamic and circulatory effects of a 12–14 mmHg capnoperitoneum are generally not clinically relevant (grade A). Due to the hemodynamic changes in ASA III–IV patients, however, invasive measurement of blood pressure or circulating volume should be considered (grade A). These patients also should receive adequate preoperative volume loading (grade A), beta-blockers (grade A), and intermittent sequential pneumatic compression of the lower limbs, especially in prolonged laparoscopic procedures (grade C). If technically feasible, gasless or low-pressure laparoscopy might be an alternative for patients with limited cardiac function (grade B). The use of other gases (e.g., helium) showed no clinically relevant hemodynamic advantages (grade A).

Carbon dioxide (CO_2) pneumoperitoneum causes hypercapnia and respiratory acidosis. During laparoscopy, monitoring of end-tidal CO_2 concentration is mandatory (grade A), and minute volume of ventilation should be increased in order to maintain normocapnia. Increased intraabdominal pressure and head-down position reduce pulmonary compliance and lead to ventilation-perfusion mismatch (grade A). In patients with normal lung function, these intraoperative respiratory changes are usually not clinically relevant (grade A). In patients with limited pulmonary reserves, capnoperitoneum carries an increased risk of CO_2 retention, especially in the postoperative period (grade A). In patients with cardiopulmonary diseases, intra- and postoperative arterial blood gas monitoring is recommended (grade A). Lowering intraabdominal pressure and controlling hyperventilation reduce respiratory acidosis during pneumoperitoneum (grade A). Gasless laparoscopy, low-pressure capnoperitoneum, or the use of helium might be an alternative for patients with limited pulmonary function (grade B). Laparoscopic surgery preserves postoperative pulmonary function better than open surgery (grade A).

Recommendation 3: Contraindications: cardiopulmonary status

Invasive monitoring of blood pressure and blood gases is mandatory in ASA III–IV patients (Recommendation: Grade A, no consensus: 91% agreement among experts). Low-pressure (<12 mm Hg) pneumoperitoneum is advocated in ASA III–IV patients (Recommendation: Grade B).

Obesity

Intraoperative ventilation of obese patients is more often problematic than in normal-weight patients, largely because the static pulmonary compliance of obese patients is 30% lower and their inspiratory resistance is 68% higher than normal [10]. The respiratory reserve of obese patients is thus reduced, with a tendency to hypercarbia and respiratory acidosis.

Obesity also reduces the technical feasibility of the laparoscopic approach. In obese patients, anatomical planes are less clear. This increases the level of difficulty of the dissection and prolongs operation time. Retraction of the small intestine and fatty omentum are more difficult and prevent easy exposure of the vascular pedicle at the base of the colonic mesentery in all parts of the colon. The routine use of hand-assisted laparoscopy may facilitate this.

Pandya et al. [11] have shown that the conversion rate is higher in patients with a body mass index (BMI) >29 due to increased technical difficulties. A similar conclusion was reached by Pikarsky et al. who reported a higher conversion rate in patients with a BMI >30 [12].

There is insufficient evidence in the literature to indicate which method should be preferred. Also, in conventionally operated patients, complication rates rise with increasing BMI. In particular, ventilatory complications and wound infections are encountered in these patients. We found no study comparing laparoscopic to open colon-cancer surgery in the obese. For laparoscopic cholecystectomy, many studies have demonstrated similar complication rates after open and laparoscopic surgery [13, 14, 15, 17, 18].

Statement 4: Contraindications: obesity

Obesity is not an absolute contraindication, but the rates of complication and conversion are higher at a BMI >30 (Level of evidence: 2c, no consensus: 93% agreement among experts).

Characteristics of the tumor

Radical resection of colonic cancer is essential for cure. Atraumatic manipulation of the tumor and wide resection margins (longitudinal and circumferential) are the basic elements of curative surgery [19]. Laparoscopic radical resection of locally advanced colorectal tumors is problematic because adequate laparoscopic atraumatic dissection of bulky tumors is difficult. Furthermore, laparoscopic resection of adjacent involved organs or the abdominal wall compounds the technical problem. Hence, the role of laparoscopic surgery in patients with T4 cancers remains controversial. The majority of the experts consider T4 colonic cancer an absolute contraindication to laparoscopic resection; en bloc laparoscopic resection is possible only in a limited number of patients. The routine use of hand-assisted laparoscopy may change this in the future.

The laparoscopic approach is useful for palliative resections of colonic cancer. Most experts do not consider peritoneal carcinomatosis to be a contraindication for laparoscopic surgery.

Recommendation 5: Contraindications: tumor characteristics

Potentially curative resections of colon cancer suspected of invading the abdominal wall or adjacent structures should be undertaken by open surgery (Level of evidence: 5, Recommendation: Grade D, no consensus: 83% agreement among experts)

Adhesions

Adhesions account for 17% of all conversions. However, prior abdominal operation appears to play a less important role in the completion rate of laparoscopic colon resection, as reported by Pandya et al. [11]. In this study, conversion rates did not differ between patients who had previous abdominal operation and those who did not. In this series of 200 patients, 52% of whom had had a previous laparotomy, only five required conversion to laparotomy because of extensive intraabdominal adhesions. Hamel et al. [20] compared the morbidity rate following right hemicolectomy between patients with and without prior abdominal operation. The complication rates for the two groups were similar despite the presence of more adhesions in the previously operated group.

To our knowledge, no studies have been published comparing laparoscopic to open surgery for patients with previous abdominal operation.

Statement 6: Contraindications: adhesions

Adhesions do not appear to be a contraindication to laparoscopic colectomy (Level of evidence: 4).

Localization

Half the experts do not recommend laparoscopic resections of the transverse colon and the splenic flexure. The omentum, which is adherent to the transverse colon, renders dissection of the transverse colon difficult. Mobilization of a tumor at the splenic flexure can be very demanding.

Operative technique

Anesthesia

Nitrous oxide, when employed as inhalational anesthetic, does not cause intestinal distention assessed by girth of transverse colon and terminal ileum at the beginning and end of the procedure [21]. The first study investigating the usefulness of nitrous oxide during laparoscopic surgery was completed by Taylor et al. [22]. In one group, isoflurane with 70% N_2O in oxygen (O_2) was used, in the other; isoflurane in an air/O_2 mixture was used during laparoscopic cholecystectomy. No significant intraoperative differences were found between the two groups with respect to operating conditions or bowel distension. However, the consequences of the use of nitrous oxide during longer laparoscopic procedures have not been investigated.

Most experts employ general anesthesia without epidural analgesia.

Pneumoperitoneum

Recommendations regarding the creation of a pneumoperitoneum are given in the EAES consensus statement of 2002 [9].

Trocar positions

Positioning of the trocars is based on the experience and preference of the individual surgeon. For right hemicolectomies, 50% of experts use four trocars, 30% use three trocars, and 20% use five trocars. Most of them extract the specimen through an incision made at the site of the umbilical trocar. At the umbilicus, a 10–12-mm trocar is placed. A 10-mm trocar is placed suprapubically and another trocar in the epigastric region by 70% of authors. Some experts place a 5-mm trocar at the left iliac fossa or at the right subcostal space.

For left hemicolectomy and for sigmoid resection, trocars are positioned at almost the same sites. Thirty percent of experts perform these procedures using a hand-assisted technique. Five trocars are used by $>70\%$ of experts. A 10–12-mm trocar is placed at the umbilicus; two 10-mm trocars are placed by 80% of experts in the right iliac fossa and in the right suprapubic region. The incision for specimen extraction is made at the left iliac fossa, or, if the hand-assisted technique is used, the specimen is extracted through the hand port incision, usually in the upper lateral abdomen. For left hemicolectomy, the specimen is extracted through a suprapubic incision or through an incision at the left iliac fossa.

Statement 7: Placement of trocars

Placement of trocars is based on the experience and the preference of the individual surgeon (Level of evidence: 5).

Camera

There is unanimous agreement about the use of a three-chip camera, because of its better resolution. The laparoscope can be 30° or 0°, depending on the surgeon's preference. Two experts use a flexible videolaparoscope. The camera is hand-held by most experts. Mechanical and robotic devices are available, but they are used by $<10\%$ of experts.

Recommendation 8: Videoscopic Image

High-quality videoscopic imaging is strongly recommended (Level of evidence: 5, Recommendation: Grade D).

Prevention of port site metastasis

Port site metastases after laparoscopic resection of colon cancer have caused great concern in the surgical community. Therefore, the causative mechanisms in the occurrence of port site metastases has become an important subject for experimental research. Many mechanisms have been proposed and have been subject of extensive research [23]. However, so far no conclusive pathogenesis of port site metastases has been established. We will discuss the most common preventive measures for port site metastases and their pathogenesis. No levels of evidence and grades of recommendation are given for each individual measure because most evidence is derived from experimental research and there is no consensus among the experts on which measures to use.

Surgical experience

The incidence of port site metastases has decreased dramatically with growing experience. The initial incidence of port site metastases of 21% has dropped to < 1% (see Port-site metastases). Surgical experience thus appears the main determinant for the occurrence of port site metastases.

Wound protectors

Experimental studies have shown that tumor growth is increased at the site of extraction of a malignant tumor [24]. All experts protect the abdominal wall or place the specimen in a plastic bag prior to extraction to prevent tumor cell implantation and growth. However, port site recurrences have been reported after extraction of a right colonic cancer that was placed in a plastic bag [25]. Therefore, wound protection is considered safer.

Gasless laparoscopy

In view of the possibility that a positive pressure pneumoperitoneum may be responsible for wound tumor deposits, some surgeons have suggested the use of gasless laparoscopy. In this respect, experimental findings on gasless laparoscopy are controversial. Bouvy et al. [24] and Watson et al. [26] reported a significant decrease in the occurrence of port site metastasis when gasless laparoscopy was used in an animal model. Gutt et al. [27] and Iwanaka et al. [28] could not confirm these observations. Wittich et al. reported in an experimental study that tumor growth was proportional to the insufflation pressure [29]. Hence, low insufflation pressures may reduce the risk of dissemination.

Different types of gas

Carbon dioxide attenuates the local peritoneal immune response, which might enhance the risk of tumour cell implantation and tumor growth in the traumatized tissues[28, 30–34]. Neuhaus et al. [35], Jacobi et al. [36], and Bouvy et al. [37] assessed tumor growth in animals after abdominal insufflation with different gases. Only helium significantly reduced the rate of wound metastasis. However, the clinical implications of the use of helium in humans have not been explored fully.

Wound excision

Because cancer cells can implant in wounds during surgery, it might be expected that excision of the wound edges would reduce the rate of neoplastic wound recurrences. This has not been confirmed in animal studies. Wu et al. [38] reported a reduction in port site metastases rates from 89% to 78% after wound excision, whereas Watson et al. reported that wound excision was followed by a significant increase of wound recurrence [39].

Irrigation of peritoneal space and port site

Irrigation of the peritoneal cavity with various solutions to reduce the incidence of peritoneal and port site metastases has been studied mostly in animal models. These studies have shown that peritoneal irrigation with povidone-iodine [40, 41], heparin [42], methotrexate [40], and cyclophosphamide [28] all reduced the rate of port site metastasis. Intraperitoneal tumor growth and trocar metastases were suppressed by the use of taurolidine in a rat model [36, 43, 44]. Eshraghi et al. [45] irrigated the port sites with distilled water, saline, heparin, and 5-FU. They found that 5-FU reduced the recurrence rate. Half of the experts irrigate the port sites with either betadine, distilled water, or tauroline.

Trocar fixation

Tseng et al. [46] showed in an experimental study that gas leakage along a trocar (“chimney effect”) and tissue trauma at the trocar site predisposed to tumor growth. However, the chimney effect has never been validated clinically.

Aerosolization

In experimental studies [47, 48], aerosolization occurs only when very large numbers of tumor cells are present in the abdominal cavity. The clinical significance of the aerosolization of tumor cells has not been proven. Some experts advocate desufflation of the pneumoperitoneum at the end of the operation before removal of the ports.

No-touch technique

The no-touch technique is based on the risk of dislodging tumor emboli during manipulation of the colorectal carcinoma. The value of the no-touch technique in colon surgery remains controversial. An improvement in the 5-year survival was reported by Turnbull et al. in a retrospective analysis [49]. In the only prospective randomized trial, which evaluated 236 patients, Wiggers et al. [50] showed that the no-touch technique did not impart a significant 5-year survival advantage. The absolute 5-year survival rates were 56.3% and 59.8% in the conventional arm and no-touch surgical groups, respectively. In the conventional group, more patients had liver metastases and the time to metastasis was shorter, but differences in survival were not statistically significant.

Bowel washout

Studies have shown that viable tumor cells exist in the lumen of the colon and rectum. Rectal washout may thus reduce risk of recurrence, but the potential benefit remains unproven [19]. Exfoliated tumor cells have been detected in resection margins, rectal stumps, and circular stapling devices [51–53]. Furthermore, the viability and proliferative and metastatic potential of exfoliated malignant colorectal cells have been confirmed [52, 53], Several washout solutions, including normal saline, have been shown to eliminate exfoliated malignant cells in the doughnut of rectal tissue from circular staplers [54]. Despite these observations, there is no conclusive evidence that bowel washouts reduce local recurrence and hence no data to support their use in surgery for colon cancer.

Statement 9: Preventive measures for port site metastasis

Proper surgical technique and practice reduce the likelihood of port site metastasis (Level of evidence: 5).

Tumor localization

Preoperative tumor localization is important in the laparoscopic resection of colonic cancer because intraoperative localization by palpation of the colon for tumors that are not visible on the serosal side is not possible unless the hand-assisted laparoscopic surgery (HALS) technique is used. The risk of incorrect tumor localization includes resection of the wrong bowel segment or less than radical resection because of insufficient proximal or distal margins [55–57].

Many colonoscopic techniques are used for marking the site of a tumor. Two of these, metal clip placement [58, 59] and tattooing [60, 61], are most commonly used. Tumor localization is advisable except for tumors located near the ileo-cecal valve, which forms a clear landmark during colonoscopy [62]. Special equipment is needed for clip placement. Before surgery, plain abdominal radiography is performed to exclude the migration of clips. During surgery, the clips are identified by intraoperative ultrasound or fluoroscopy. Hence, this is an expensive and time-consuming technique [63], although it is very reliable [59, 64].

Intra-operative colonoscopy is an alternative modality to localize the colonic lesion. However, this technique can induce distention of the colon and small bowel, particularly in right-sided lesions [65]. The colonoscopic tattooing technique with india ink or methylene blue is efficient. Tattoo injection with ink can be carried out at the time of the first colonoscopy because ink remains in place for several weeks. It is important to inject the dye in all quadrants, at an angle of 45°, and to mark the oral and aboral margins of the lesion. A thick omentum or tattooing along the mesocolic margin can mask a tattoo such that localization fails. Reported success rates for detection of the tumor after tattooing vary between 78.6% and 98% [61, 66]. The reported morbidity rate for tattooing is 0.22% [67]. In this review, only one patient was found in whom overt clinical complications developed. Injection into the peritoneal space has been reported in 0.5–8% [63, 68].

Recommendation 10: Intraoperative localization of tumor

Preoperative tattooing of small colonic tumors is advised. The alternatives are intraoperative colonoscopy, or pre-operative colonoscopic clipping followed by peroperative fluoroscopy, or ultrasonography (Level of evidence: 5, Recommendation: Grade D).

Hand-assisted or laparoscopic-assisted approach

Basically, three different techniques are described for laparoscopic colon resection: totally laparoscopic, laparoscopic-assisted, and hand-assisted colectomy.

During totally laparoscopic procedures, the resected specimen is removed through the anus. It can be performed during low anterior resection or sigmoidectomy. The anastomosis is done laparoscopically using a circular stapler introduced through the anus. Totally laparoscopic procedures have been abandoned, largely because early experience indicated a high recurrence rate at the extraction site and no apparent advantage [69].

In laparoscopic-assisted colon resection, part of the procedure is performed in an open fashion through an incision of the abdominal wall made for the extraction of the resected specimen. This is the most common procedure for all colectomies.

Hand-assisted laparoscopic surgery (HALS) is an alternative to laparoscopically assisted colectomy. This procedure enables the surgeon to use his or her hand, with the dual benefit of magnified view and restoration of the tactile sense by the internal hand, which also provides atraumatic retraction and effective control of sudden bleeding. In addition, the internal hand is able to locate small tumors that are not visible from the serosal aspect.

With the early hand access devices, maintenance of the pneumoperitoneum was difficult, but this problem has been resolved with the second generation of hand access devices [70]. HALS appears to be at least as effective as the laparoscopically assisted technique in terms of operative time, conversion rate, and postoperative outcome [71]. Only two experts use HALS for laparoscopic colectomy.

Dissection of mesocolon

Most experts dissect the mesocolon before taking down the lateral attachments of the colon. Fifty-four percent of experts use a vascular stapling device, 27% employ an external knotting technique, and 18% use clips to ligate the large-caliber mesocolic vessels. Most experts dissect the mesocolon from medially to laterally over Toldt's fascia. All agree that the surgeon must know both approaches to be able to deal with a difficult problem during the procedure.

For right hemicolectomy, the mobilization of the bowel is always performed laparoscopically. Dissection of the mesocolon and bowel transection can both be performed laparoscopically or after the colon has been exteriorized. Transection of the ileum is performed laparoscopically by 71% of experts. Aboral transection of the colon, as well as the anastomosis, is performed after exteriorization. In left hemicolectomy, dissection of the mesocolon, mobilization of the colon, and transection of the aboral colon are done laparoscopically. The anastomosis is performed using a circular stapler introduced through the anus by 66% of experts. Others perform a stapled or hand-sewn anastomosis after exteriorization of the colon. No preference exists for either end-to-end, end-to-side, or side-to-side anastomosis.

Sigmoidectomy involves the same steps as left hemicolectomy, but all experts use a circular stapler for the anastomosis.

Recommendation 11: Dissection of mesocolon

Dissection of the mesocolon from medial to lateral is the preferred approach in laparoscopic colon surgery (Level of evidence: 5, Recommendation: Grade D).

Learning curve

"Learning curve" can be defined in various ways. Simons et al. considered the learning curve completed when the operative time stabilizes and does not vary by more than 20 min [72]. Schlachta et al. [73] demonstrated that operating time, intraoperative complications, and conversion rates decline after the performance of 30 colorectal resections. Bennett et al. [74] reported that experience plays an important role in reducing complication rates and has less impact on reducing the operating time. Lezoche et al. reported that the conversion rate dropped from 17% to 2% after 30 laparoscopic colectomies [75]. Many surgeons consider the learning curve for laparoscopic colonic resection to be longer than that for laparoscopic cholecystectomy.

Intraoperative results of laparoscopic resection of colon cancer

Conversion rate

Reported conversion rates in laparoscopic surgery depend on the definition of conversion, the selection of patients, and the experience of the surgeon. Conversion rates between 4% and 28% have been reported in comparative studies (Table 2.)

There is currently no standardized definition of conversion. In most studies, an operation is considered to be converted when a laparoscopic procedure was commenced but could not be completed by this approach. In two studies, a diagnostic laparoscopy was performed before every operation to establish the feasibility of a laparoscopic resection [76, 77]. If laparoscopy indicated that resection would not be possible, open surgical resection was performed. These operations were not considered as converted. In two case series, high conversion rates of 41% and 48% were reported [78, 79]. Both studies reflected a very early experience with laparoscopic surgery, and no attempt was made to select patients according to weight, tumor stage, or number of previous abdominal operations. None of the other case series that have been reviewed reported higher conversion rates [56, 76, 80–83].

In a study by Lezoche et al., conversion rates were calculated for the first 30 patients operated laparoscopically and for the consecutive 26 patients [84]. The conversion rate in the early experience group was 16.8%, whereas in the subsequent group it was 1.8%; this finding underscores the importance of experience in reducing the conversion rate. This finding was confirmed by several other reports analyzing early and later experiences with laparoscopic colon surgery [11, 56, 81, 85]. All found a clear decrease in the number of conversions as more operations were performed.

Laparoscopic colectomies are converted for a variety of reasons. Locally advanced bulky or invasive tumors, adhesions, and technical problems account for most conversions (Table 2). Because many conversions are for invasive or bulky tumors, improved preoperative selection of patients based on more accurate clinical staging may decrease conversion rates. Preoperative CT or MRI scanning can provide more information on the localization of the tumor and the invasion of surrounding structures.

Statement 12: Conversions

Laparoscopic colectomy is converted to open surgery in 14% (0–42%) of cases. The most common causes of conversion are tumor invasion of adjacent structures or bulky tumor, adhesions, and technical failure (Level of evidence: 3a).

Duration of surgery

In general, laparoscopic resection of colonic cancer takes longer to perform than open resection. Although operating time decreases with increasing experience [75, 78, 81, 84, 86], it is difficult to compare operating times between open and laparoscopic resections for colon cancer because most studies include a wide variety of procedures and do not specify per type of resection performed. Studies that included rectal procedures reported longer operating times [77, 87, 88].

Reported operating times vary between 140 and 251 min for laparoscopic colorectal resections and 120 and 175 min for open surgery (Table 3). In some studies, benign lesions were also included [77], and rectal procedures were excluded in only one RCT [89]. In two RCT [77, 87] and in five nonrandomized comparative studies, the intention-to-treat principle was violated [75, 88, 90–92], resulting in selection bias, possibly favoring the laparoscopic group.

Statement 13: Duration of surgery

Laparoscopic colectomy requires more operating time than open colectomy (Level of evidence: 2a).

Statement 14: Extent of resection

For a laparoscopic oncological resection to be as safe as an open resection, the extent of resection of colonic and lymphatic tissue should not differ from that of open colectomy. All RCT report similar numbers of lymph

Table 2. Reported conversion rates in studies on laparoscopic resection of colorectal cancer

Study	n	Conversion rate	Cause
1			
Week [115]	58/228	25	One advanced disease,three positive margins, 10 inability to visualize structures, four inability to mobilize colon, 12 adhesions, four intraoperative complications, two associated complicating disease, 12 other
Schwenk [111]	0/30	0	After diagnostic laparoscopy
Milson [77]	4/59	7	Two bowel distension, one tumor too low, one adhesions
Delgado [5]	18/129	14	15 invasion of adjacent organs, one adherence, two NS
Cure [87]	7/25	28	Three tumor fixation to adjacent organs, three extensive adhesions, one abscess around ureter
Stage [94]	3/18	17	Three extensive tumor growth
Lacy [93]	4/25	16	Four invasionof small bowel
3			
Lezoche [84]	6/140	4	Two hemorrhage, two anastomotic defects, one obesity, one inadequate splenic flexure mobilization
Feliciotti [126]	5/104	4.8	Two anastomotic defects, one obesity, one Inadequate splenic flexure mobilization, hemorrhage
Bouvet [88]	38/91	42	Twelve adhesions,eight poor exposure, five extensive tumor growth, three excessive procedure time two bleeding, two inability to identify the ureter, one inadequate distal margin, one equipment failure, four combination of factors
Hong [112]	12/98	12	Five adherence, five size of tumor, two adhesions
Psaila [117]	3/25	12	NS
Khalili [90]	6/80	8	Three extensive tumor, two adhesions, one intraoperative bleed
Pandya [11]	47/200	23.5	Six hypercarbia, two unclear anatomy, two stapler misfiring, five too ambitious, six bleeding, seven cystotomy, two enterotomy, five adhesions, three obesity, 10 size/invasion tumor, five phlegmon
Bokey [95]	6/34	18	One injury cecum, one adhherence, one adhesions, one hypercapnia, two lack of progress
Franklin [116]	8/192	4.2	Seven large invasive tumor, one bleed
Santoro [114]	0/50	0	–
Leung [92]	8/50	4	Two adhesions, two bleeding, three large/invasive tumors, one low tumor
Van Ye [99]	1/15	6.7	one adhesions
Leung [104]			
4			
Schiedeck [152]	25/399	6.3	NS
Bokey [103]	9/66	14	Two lack of progress, two adherence, one adhesions, one cecal injury, one hypercapnia, one ureter not identinfined, one bleed
Fleshman [153]	58/372	15.6	Not specified
Franklin [154]	3/50	6	Three bulky/invasive tumor
Poulin [155]	12/131	9	Six fixed tumor, three adhesions, one oncologic resection impossible, one hemorrhage, one perforation small bowel
Leung [108]	54/201	26.9	Twenty two conversions after diagnostic laparoscopy (not further specified) Invaisve or bulky tumor: 36% Adhesions: 18% Technical problem: 22% (twelve lack of progress, eighteen poor exposure, eight hypercarbia, six anastomotic problem, two bowel distension, six inadequate mobilization, one equipment failure)
Total	395/2812	14%	Bleed: 7% Safe oncologic resection imossible: 2% Visceral injury: 3% Obesity: 2% Others: 10%

NS, not specified

nodes harvested in laparoscopic and open surgical specimens. Also, the length of the retrieved bowel segments and tumor-free margins were comparable [5, 77, 87, 93, 94] (Table 4).

In nonrandomized comparative studies, no differences between open and laparoscopic groups were found for number of lymph nodes, length of the retrieved specimen, tumor-free proximal and distal margins, and total length of specimen. In two studies, a smaller distal resection margin was recorded [88, 95]. However, in these studies, the mean distal tumor-free resection margins were still 6 and 10 cm, respectively, which is oncologically acceptable.

There are reports of laparoscopic colon resections not containing the primary tumor or missing a synchronous second colonic carcinoma [55–57]. This type of result underscores the importance of tumor localization by either tattooing the tumor with ink or intraoperative colonoscopy.

The extent of laparoscopic lymphadenectomy and bowel resection is similar to those obtained by open colectomy (Level of evidence: 2b).

Clinical outcome

Short-term outcome

Morbidity

The reported morbidity and mortality rates for open conventional colorectal surgery range from 8% to 15% and 1% to 2%, respectively [96]. Serious complications

Table 3. Duration of Surgery

Study	Laparoscopic	Open	*p* value
2			
Lacy [89]	142 ± 52	118 ± 45	0.001
Hewitt [102]	165 (130–300)	107.5 (90–150)	0.02
Milsom [77]	200 ± 40	125 ± 51	< 0.0001
Delgado [5]	< 70 yr: 144 ± 40	122 ± 45	0.005
	> 70 yr: 150 ± 60	119 ± 51	0.001
Cure [87]	210 (128–275)	138 (95–240)	< 0.05
Stage [94]	150 (60–275)	95 (40–195)	0.05
Lacy [93]	148.8 ± 45.5	110.6 ± 49.3	0.006
Schwenk [156]	219 ± 64	146 ± 41	< 0.01
3			
Lezoche [84]	RHC 190 (90–330)	140 (90–280)	0.03
	First 30: 226 (140–330)		
	Last 20: 153 (90–240)		
	LHC 240 (150–480)	190 (130–340)	0.04
	First 30: 260 (150–480)		
	Last 20: 210 (150–320)		
Bouvet [88]	240 (150–516)	150 (60–376)	< 0.01
Fukushima [150]	231 ± 23	169 ± 20	NS
Hong [112]	140 ± 49.5	129 ± 53.5	NS
Psaila [117]	179 ± 41	123 ± 41	< 0.05
Khalili [90]	161 ± 7	163 ± 8	NS
Lezoche [75]	Overall 251 (90–480)	175 (90–340)	< 0.001
	RHC 203 (90–330)	140 (90–280)	< 0.001
	LHC 282 (150–480)	190 (130–340)	< 0.001
Marubashi [91]	RHC 211.9 (134–330)	148.7 (104–173)	< 0.05
Leung [92]	196 ± 44.4	150 ± 61.1	< 0.001

NS, not significant; RHC, right hemicolectomy; LHC, left hemicolectomy
Results given as mean ± SD or median (range)

include anastomotic leakage, bowel obstruction, and abdominal and pulmonary infection.

Table 5 summarizes the studies describing morbidity following laparoscopic colectomy. Data from the RCT indicated a significantly lower overall complication rate after laparoscopic surgery [5, 89, 93]. In a subset analysis comparing laparoscopic to open resection, reduction of postoperative morbidity after laparoscopic resection was more pronounced than in patients under 70 years of age [5].

Morbidity of laparoscopic resection of colonic cancer has not been reported in sufficient detail by most authors [97]. Specific complications of laparoscopic surgery involve vascular and visceral injuries, trocar site hernias [98, 99], and transection of the ureter [79]. Vascular injuries may be caused by blind introduction of the Veress needle or first trocar [78, 79, 97, 100]. Winslow et al. reported incisional hernias at the extraction site in 19% after laparoscopic colectomy, whereas incisional hernias occurred in almost 18% after open colectomy [101].

Experience is an important factor in preventing complications, as shown in three studies that reported lower morbidity with increasing experience [56, 74, 85]. A recent systematic review [96] analyzed morbidity as reported in 11 studies [92–94, 102–109] (Table 6).

The infectious complications of laparoscopic colectomy have not been assessed by large-scale prospective randomized studies. Wound infection at the extraction site was encountered in 14% of patients after laparoscopic colectomy vs 11% of patients after open colectomy [101].

Statement 15: Morbidity

Morbidity after laparoscopic colectomy does not differ from that after open colectomy (Level of evidence: 2b).

Mortality

Mortality rates, defined as death within 30 days after surgery, are similar for both open and laparoscopic colectomy. However, no randomized controlled trials on laparoscopic vs open colectomy have yet been conducted with sufficient numbers to distinguish small differences. In two RCT, a 0% mortality rate was reported for both open and laparoscopic procedures [102, 110]. In the RCT by Schwenk et al. [111], one death occurred in the conventional group and none in the laparoscopic group. In another RCT, three deaths occurred, but this study failed to report to which group these patients were assigned to and the causes of death [94].

In nonrandomized reports, mortality was reported in only five studies [95, 104, 112–114]. None of these studies showed any significant differences between the open and laparoscopic groups, although the cohorts were too small to detect small differences.

Statement 16: Mortality

Mortality of laparoscopic colectomy appears similar to that of open colectomy (Level of evidence: 2b).

Table 4. Number of lymph nodes and extent of resection

Study	No. of lymph nodes Laparoscopic	Resection margins (cm) Open	*P* value	Laparoscopic	Open	*p* value
2						
Milsom [77]	19[a]	25*	–	Clear in all	Clear in all	
Delgaddo [5]	< 70 yr 9.6	10.5	NS			
	> 70 yr 12.2	10.5	NS			
Cure [87]	11	10	NS	Length 26	25	–
Stage [94]	7	8	–	Margins 4	4	
Lacy [93]	13	12.5	NS			
3						
Lezoche [84]	RHC 14.2	13.8	NS	Length 28.3	29.1	NS
	LHC 9.1	8.6	NS	Length 22.9	24.1	NS
				LHC TFM 5.2	5.3	NS
Bouvet [88]	8	10	NS	Prox 10	10	NS
				Dist 6	9	0.03
Hong [112]	7	7	NS	Dist 7.9	7.2	NS
Koehler [113]	14	11	–	Length 24.1	22.6	–
				Prox 13.2	10.1	–
				Dist 7.9	8.6	–
Psaila [117]	7.0	7.7	NS			
Khalili [90]	12	16	–			
Lezoche [75]	10.7	11	NS	Length 26.8	29.4	NS
				LHC TFM 5.2	5.3	NS
Marubashi [91]				LoD 1.7	2.25	< 0.01
Bokey [95]	17	16	NS	Prox 10.1	11.0	NS
				Dist 10.0	13.4	0.03
Franklin [116]	NA	NA	NS	NA	NA	NS
Santoro [114]						
Leung [92]	9[a]	8[a]		Dist 3[a]	3.5[a]	

NS, not significant, NA, not available; Length, length of resected specimen; Prox, proximal resection margin; Dist, distal resection margin; LHC, left hemicolectomy; RHC, right hemicolectomy; TFM, tumor-free margin; LoD, level of dissection
Results given as mean or [a] median

Table 5. Morbidity

Study	Laparoscopic (%)	Open (%)	*p* value
2			
Lacy [89]	11	29	0.001
Milsom [77]	15	15	NS
Delgado [5]	10.9	25.6	0.001
	< 70 yr 11.4	20.3	NS
	> 70 yr 10.2	31.3	0.0038
Cure [87]	1.5	5.28	NS
Stage [94]	11	0	–
Lacy [93]	8	30.8	0.04
Schwenk [111]	7	27	0.08
3			
Lezoche [84]	RHC 1.9	2.3	NS
	LHC 7.5	6.3	NS
Bouvet [88]	24	25	NS
Hong [112]	Major 15.3	14.6	NS
	Minor 11.2	21.5	0.029
Khalili [90]	19	22	NS
Lezoche [75]	13	14.3	NS
	Minor 3.6	7.5	NS
	Major 9.4	6.8	NS
Marubashi [91]	27.5	25	–
Bokey [95]	NA	NA	NS
Franklin [116]	Early 17	23.8	NA
	Late 5.2	8.9	
Santoro [114]	Early 28	28	–
	Late 12	0	
Leung [92]	26	30	NS

NS, not significant; NA, not available; LHC left hemicolectomy; RHC, right, hemicolectomy

Recovery

Length of hospital stay

Many factors determine length of hospital stay after surgery, and length of stay differs by country and hospital. Clinical condition of the patient is only one such factor. Type of insurance, social and economic status, and perception of postoperative recovery by both surgeon and patient are also important factors. Table 7 summarizes all studies comparing length of hospital stay after laparoscopic and open colectomy for cancer. The COST trial reported by Weeks et al. [115] is currently the multicenter RCT with the highest power and most published data. In this trial, a highly significant shorter hospital stay was found after laparoscopic colectomy (5.6 ± 0.26 vs 6.4 ± 0.23 days, $p < 0.001$), even though the analysis was performed on an intention-to-treat basis and patients converted to open operation were included in the laparoscopic group.

Six other RCT reported on length of hospital stay [5, 77, 87, 93, 94, 102]. In four RCT, a significant earlier hospital discharge was reported for the laparoscopic group [5, 87, 93, 94]. In one RCT with a sample size of 16, no statistical analysis was performed [102]. Median and range of length of hospital stay did not differ in this study (6 [5–7] vs 7 [4–9] days). In one RCT, the difference was not significant [77].

In the nonrandomized comparative studies, hospital stay after laparoscopic surgery varies from 5.7 to 18.7 days

Table 6. Complication rates in an analysis of 11 studies

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

Table 7. Length of hosipital stay (in days)

Study	Laparoscopic	Open	*p* value
1			
Week [115]	5.6 ± 0.26	6.4 ± 0.23	< 0.001
2			
Hewitt [102]	6 (57)	7 (4–9)	–
Milsom [77]	6.0 (3–37)	7.0 (524)	NS
Delgado [5]	< 70 yr 5	7	0.0001
	> 70 yr 6	7	0.0009
Curet [87]	5.2	7.3	< 0.05
Stage [94]	5 (3–12)	8 (5–30)	0.01
Lacy [93]	5.2 ± 1.2	8.1 ± 3.8	0.0012
3			
Lezoche [84]	RHC 9.2	13.2	0.001
	LHC 10.0	13.2	0.001
Bouvet [88]	6 (2–35)	7 (4–52)	< 0.01
Hong [112]	6.9 ± 5.4	10.9 ± 9.3	0.003
Koehler [113]	8.1 (6–14)	15.3 (9–23)	–
Psaila [117]	10.7 ± 4.7	17.8 ± 9.5	0.001
Khalili [90]	7.7 ± 0.5	8.2 ± 0.2	NS
Lezoche [75]	10.5	13.3	0.027
Marubashi [91]	18.7	35.8	< 0.0001
Franklin [116]	< 50 yr 5.2 (2.0–9.2)	9.35 (517)	–
	> 50 yr 7.84 (448)	12.85 (941)	
Leung [92]	6 (3–22)	8 (3–28)	< 0.001

NS, not significant; LHC, left hemicolectomy; RHC, right hemicolectomy
Results given as mean ± SD or median (range)

and between 8 and 35.8 days after open surgery [75, 84, 88, 90–92, 112, 113, 116, 117]. In all these studies, hospital stay was shorter in the laparoscopic group, although in three studies the differences were not significant [90, 113, 118]. Differences in hospital stay between laparoscopic and open colectomy groups vary from 1 to 7 days.

A recent article by Wilmore et al. [119] reviewed – fast-track– surgery for open procedure. Fast-track surgery is a multimodal approach that combines various techniques used in the perioperative care of patients to achieve a faster recovery and discharge after surgery. Methods include epidural or regional anesthesia, optimal pain control, early enteral feeding, and early mobilization. This Danish research group managed to shorten the postoperative hospital stay to 2 days after conventional open colectomy. So far, this approach has not been studied for patients undergoing the laparoscopic resection of colon cancer.

Statement 17: Length of hospital stay

Hospital stay after laparoscopic resection of coloncancer is shorter than after open colectomy (Level of evidence: 1a).

Postoperative pain

Postoperative pain is an endpoint that impacts on the perceived health status, quality of life, hospital stay, and resumption of normal activities. In general, less postoperative pain is perceived after endoscopic surgery than after open surgery. In one RCT, statistically significantly less pain at rest after laparoscopic resection of colonic cancer was observed for ≤30 days postoperatively, when compared to open colectomy [94]. Also pain during mobilization was reported to be less severe. The number of patients included in this trial, however, was limited and the methodology used was flawed because the intention-to-treat principle was violated. Similar results were obtained by another RCT [113]. This study showed differences in pain at rest and during mobilization for ≤12 days, but these differences were not significant. In a recent RCT, postoperative pain was analyzed using the Symptoms Distress Scale, which includes self-reported symptoms such as pain, along with the duration of use of analgesics [115]. In this study, only a shorter duration of use of analgesics was observed in the laparoscopic arm.]

Statement 18: Pain

Pain is less severe after laparoscopic colectomy (Level of evidence: 2a).

Postoperative analgesia

The need for analgesics after surgery can be measured in several ways. Table 8 summarizes all studies comparing postoperative analgesia after laparoscopic or open resection of coloncancer. Some authors assessed the number of pills or injections per day [75, 77, 92], whereas others recorded the number of days the patient needed analgesics [91, 95, 112]. In the COST trial, patients in the laparoscopic arm required parenteral and oral analgesics for a shorter period of time [115]. In another RCT, significantly less morphine was used in the laparoscopic groups only on the 1st postoperative day [77]. In all other studies, the laparoscopic group used fewer analgesics, although the difference was not always significant [75, 91, 92, 95, 102, 112, 120].

Table 8. Postoperative analgesia

Study			Laparoscopic	Open	*p* value
1					
Week [115]	Oral (d)		2.2 ± 0.15	1.9 ± 0.15	0.03
	Parenteral (d)		4.0 ± 0.16	3.2 ± 0.17	< 0.001
2					
Milsom [77]	Morphne	Day 1	0.78 ± 0.32	0.92 ± 0.34	0.02
		Day 2	0.45 ± 0.29	0.50 ± 0.31	NS
		Day 3	0.39 ± 0.32	0.36 ± 0.24	NS
Schwenk [120]	PCA (morphine)	Cumulative dose until day 4	0.78 (0.24–2.38)	1.37 (0.71–2.46)	< 0.01
Hewitt [102]	Morphine	Cumulative dose until day 2	27 (0–60)	62 (28–88)	0.04
3					
Hong [112]	Days till stop iv or im analgesia		2.7 ± 1.5	3.2 ± 2.0	0.021
Lezoche [75]	Analgesics in percentage of patients	Day 1	75%	98%	< 0.001
		Day 2	49%	91%	0.001
		Day 3	10%	71%	< 0.001
		Day 4	0.7%	49%	< 0.001
		Day 5		21%	
Marubash [91]	Days till stop epidural		2.98	4.04	< 0.05
	No. of pills		1.49	2.68	NS
Bokey [95]	Days till stop (parental analgesia)		4.4	4.9	NS
Leung [92]	No. of injections		3 (0–16)	6 (0–32)	< 0.001

NS, not significan
Results given as mean ± SD or median (range)

Table 9. Gastrointestinal function

	Flatus/defecation (d)			Bowel movement		
Study	Laparoscopic	Open	*p* value	Laparoscopic	Open	*p* value
2						
Lacy [89]				36 ± 31	55 ± 40 (h)	0.001
Milsom [77]	3 (0.8–8)	4 (0.8–14)	0.006	4.8 (1.5–8)	4.8 (1.5–14.5)	NS
Delgado [5]				< 70 yr 35 ± 36	53 ± 26	0.0007
				> 70 yr 37 ± 19	57 ± 33	0.0005
Lacy [93]	35.5 ± 15.7 h	71.1 ± 33.6 h	0.0001			
Schwenk [156]	50 ± 19	79 ± 21	< 0.01	70 ± 32	91 ± 22	< 0.01
3						
Lezoche [84]	Flatus					
	RHC 2.9	3.0	NS			
	LHC 2.7	3.5	< 0.0001			
	Defecation					
	3.5	4.0	< 0.0001			
	3.8	5.2	< 0.0001			
Hong [112]	3 ± 1.7	4.1 ± 1.8	< 0.0001	3.5 ± 2	4.9 ± 2.1	< 0.0001
Koehler [113]	3.4 (2–5)	5.8 (3–7)	–			
Lezoche [75]	3.0	3.7	NS	3.4	4.5	0.036
Marubashi [91]	2.1	3.75	< 0.0001			
Bokey [95]	4.5	4.4	NS	4.9	5.5	NS

NS, not significant; LHO, Left hemicolectomy; RHC, right hemicolectomy Results given as mean ± SD or median (range)

Statement 19: Postoperative use of analgesics

Less analgesia is needed after laparoscopic colectomy than after open colectomy (Level of evidence: 1b).

Gastrointestinal function

Resumption of intestinal function can be measured by several parameters: time to first bowel movement, first passage of flatus or defecation (Table 9), and time to resume intake of liquid or solid foods (Table 10). In the RCT, data on passage of first flatus and defecation are consistent with a faster recovery in the laparoscopic group. In two studies, the differences were not significant [75, 103]. In all RCT, first bowel movement and resumption of diet were earlier after laparoscopic colorectal surgery.

Statement 20: Gastrointestinal function and start of postoperative oral intake

Gastrointestinal function recovers earlier after laparoscopic colectomy (Level of evidence: 2b).

Pulmonary function

Laparoscopic surgery causes less impairment of pulmonary function, enabling faster recovery. Postoperative pulmonary function after laparoscopic

Table 10. Start of postoperative oral intake

Study	Parameter	Laparoscopic	Open	*p* value
2				
Lacy [89]	Oral intake	54 ± 42	85 ± 67	0.001
Delgado [5]	Oral intake	< 70 yr 50 ± 45	59 ± 33	0.0001
		> 70 yr 59 ± 33	81 ± 48	0.002
Curet [87]	Clear liquids	2.7	4.4	< 0.05
	Regular diet	4.1	5.8	< 0.05
Lacy [93]	Oral intake	50.9 ± 20	98.8 ± 48.6	0.0001
Schwenk [156]	Regular diet	3.3 ± 0.7	5.0 ± 1.5	< 0.01
3				
Hong [112]	Fluids	2.1 ± 1.8	4.0 ± 2.0	< 0.0001
	Solid food	5.2 ± 3.1	7.1 ± 2.8	< 0.0001
Koehler [113]	Regular diet	3.2 (2–6)	6.2 (4–10)	–
Khalili [90]	Oral intake	3.9 ± 0.1	4.9 ± 0.1	0.001
Lezoche [75]				
Marubashi [91]	Oral intake	5.13	10.04	< 0.0001
Bokey [95]	Fluids	4.3	4.2	NS
	Full diet	6.9	7.6	NS
Leung [92]	Normal diet	4 (2–20)	4 (3–17)	NS
Van Ye [99]	Normal diet	4.8	7.2	0.001

Results given as mean ± SD at median (range)
NS, not significant

Table 11. Postoperative pulmonary function

Study	Parameter	Laparoscopic	Open	*p* value
1				
Schwenk [111]	FVC (p.o. day 1)	2.59 ± 1.11	1.73 ± 0.60	< 0.01
	FEV_1 (p.o. day 1)	1.80 ± 0.80	1.19 ± 0.51	< 0.01
	PEF (p.o. day 1)	3.60 ± 2.22	2.51 ± 1.37	< 0.05
	FEF 25–75% (p.o. day 1)	2.67 ± 1.76	1.87 ± 1.12	< 0.05
	SaO_2 % (p.o. day 1)	93.8 ± 1.9	92.1 ± 3.3	
2				
Milsom [77]	FEV_1 and FVC (days till 80% recovery of preoperative values)	3.0	6.0	0.01
Stage [94]	FEV_1	NA	NA	NS
	FVC	NA	NA	
	PEF	NA	NA	

p.o., postoperative; NS, not significant; NA, not available; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1; PEF, peak expiratory flow; FEF, 25–75%, forced expiratory flow at 25–75% of forced vital capacity; SaO_2, arterial oxygen saturation
Results given as mean ± SD or median (range)

cholecystectomy, as compared to the open counterpart, is improved [121]. Postoperative pulmonary function after colorectal resection has been investigated in an RCT by Schwenk et al. [111]. Parameters shown in Table 11 were measured preoperatively and at different time points postoperatively. Forced vital capacity and forced expiratory volume were more profoundly impaired in patients who underwent conventional resections than in the laparoscopic group. Similar results were found for the peak expiratory flow and the mid-expiratory phase of the forced expiratory flow. Also, the postoperative oxygen saturation was lower in the conventional group than in the laparoscopic group. Two pneumonias occurred in the conventional group vs none in the laparoscopic group. The difference was not significant, but the sample size of the study was only 30 patients.

Postoperative pulmonary function was investigated in two other RCT. Milsom et al. [122] found a significantly earlier postoperative recovery of pulmonary function after laparoscopic surgery. The RCT conducted by Stage et al. [94] showed no significant differences between the two groups in pulmonary function.

Statement 21: Postoperative pulmonary function

Postoperative pulmonary function is less impaired after laparoscopic resection of coloncancer (Level of evidence: 1b).

Return to work and daily activities

The parameters of early recovery are strongly influenced by societal and economic organization of health care within a community. This may explain the wide variability between studies. Only in randomized trials can one assume that these factors are evenly distributed in both

Table 12. Overall survival rates

Study	Follow-up	Laparoscopic (%)	Open (%)	*p* value
2				
Lacy [89]	43 mo	82	74	NS
3				
Leung [104]	21.4 mo (median)	90.9 (*n* = 28)	55.6 (*n* = 56)	NS
Leung [92]	32.8 mo (median)	67.2 (*n* = 50)	64.1 (*n* = 50)	NS
Khalili [90]	19.6 mo	87.5 (*n* = 80)	85 (*n* = 90)	NS
Santoro [114]	5 yr	72.3 (*n* = 50)	68.8 (*n* = 50)	NS
Hong [112]	Lap 30.6 mo Open 21.6 mo	NA (*n* = 98)	NA (*n* = 219)	NS
4				
Delgado [157]	42 mo	AR 83, SR 87 (*n* = 31)		
Cook [158]	Until patient's death	20 (*n* = 5)		
Hoffman [159]	2 yr	Node–: 92 (*n* = 89) Node +: 80%		
Molenaar [160]	3 yr	All: 59, by Dukes' stage (*n* = 35): A = 86, B = 66, C = 68, D = 0		
Quattlebaum [161]	8 mo	90 (*n* = 10)		
Poulin [155]	Stage I–III: 24 mo Stage IV: 9 mo	81		

NS, not significant; NA, not available; AR, anterior resection; SR, sigmoid resection

Table 13. Disease-free survival rates

Study	Follow-up	Laparoscopic (%)	Open (%)	*p* value
2				
Lacy [89]	43 mo	91	79	0.03
3				
Leung [104]	5 yr	95.2	74.7	NS
Leung [92]	4 yr	80.5	72.9	NS
Feliciotti [126]	48.9 mo	86.5	86.7	NS
Lezoche [84]	42.2 mo 42.3 mo	RHC 78.3 LHC 94.1	75.8 86.8	NS
Bouvet [88]	26 mo	93	88	NS
Santoro [114]	NA	73.2	70.1	NS
Hong [112]	Lap 30.6 mo Open 21.6 mo	NA	NA	NS
Franklin [116]	5 yr	87	80.9	NS
4				
Delgado [157]	42 mo	AR: 78 SR: 70		
Hoffmant [159]	2 yr	Node–: 96 Node +: 79		

NS, not significant; NA, not available

groups. None of the available randomized trials addressed this topic.

Long-term outcome of laparoscopic colectomy

Overall and disease-free survival

Recently, Lacy et al. published the results of their single-center randomized controlled trial on laparoscopic curative resection of coloncancer [89]. In this study of 219 patients, 111 underwent laparoscopic colectomy. A significantly better 3-year cancer-related survival was found in the laparoscopically operated patients than in the open group (91% vs 79%, respectively). This difference in survival could be attributed mainly to the markedly better survival in stage III coloncancer patients. Follow-up data of large multicenter randomized controlled trials the (CLASICC [123], COST [124], and COLOR [125] trials) will provide a more definitive assessment of survival after laparoscopic vs open colon resections.

In smaller nonrandomized comparative studies, no significant differences in disease-free and overall survival have been observed between open and laparoscopic patient groups (Tables 12 and 13). No significant differences were found between open and laparoscopically operated patients in a nonrandomized matched control study with 5-year follow-up [104]. Another study using historical controls also showed no difference in long-term survival, with survival rates of 64.1% and 67.2% in the open and laparoscopic arms, respectively [92]. In a

Table 14. Port site metastasis after resection of colorectal carcinoma

Study	Design	*n*	Follow-up	PSM
Lacy [89]	RCT	111	Median 43	1
Milsom [77]	RCT	42	Median 18	0
Lacy [110]	RCT	31	21.4	0
Ballantyne [162]	Registry	498	NA	3
Fleshman [163]	Registry	372	NA	4 (1.3%)
Rosato [164]	Registry	1071	NA	10 (0.93%)
Vukasin [165]	Registry	480	> 12	5 (1.1%)
Schledeck [152]	Registry	399	Mean 30	1 (0.25%)
Leung [108]	Prospective	217	Mean 19.8	1 (0.65%)
Poulin [155]	Prospective	172	Mean 24	0
Franklin [116]	Prospective	191	> 30	0
Bouvet [88]	Prospective	91	26	0
Feliciottl [126]	Prospective	158	Mean 48.9	2
Bokey [103]	Retrospective	66	Median 26	1 (0.6%)
Fielding [86]	Retrospective	149	NA	2 (1.5%)
Gellman [166]	Retrospective	58	NA	1 (1.7%)
Hoffman [159]	Retrospective	39	≥24	0
Huscher [80]	Retrospective	146	Mean 15	0
Leung [92]	Retrospective	50	> 32	1
Khalili [90]	Retrospective	80	Mean 21	0
Kwok [167]	Retrospective	83	NA	2 (2.5%)
Leung [108]	Retrospective	179	Mean 19.8	1 (0.65%)
Lord [98]	Retrospective	71	Mean 16.7	0
Lumley [82]	Retrospective	103	NA	1 (1.0%)
Khalili [90]	Retrospective	80	Mean 19.6	0
Guillou [168]	Retrospective	59	NA	1 (1.7%)
Larach [56]	Retrospective	108	Mean 12.6	0
Croce [169]	Retrospective	134	NA	1 (0.9%)
Kawamura [170]	Retrospective	67 (gasless)	NA	0
		5305		38 (0.72%)

RCT, randomized controlled trial; NA, not available; PSM, port site metastases

further six comparative studies, no differences of overall survival were found between laparoscopic and open resections of coloncancer [84, 88, 112, 114, 116, 126].

Statement 22: Overall and cancer-related disease-free survival

Cancer-related survival after laparoscopic resection appears to be at least equal to open resection (Level of evidence: 2a).

Port site metastases after laparoscopic colectomy

Early reports of port site metastases after laparoscopic resection of colonic cancer generated considerable concern in the surgical community in the early 1990s. Initial enthusiasm for the laparoscopic approach to coloncancer was replaced by skepticism. Abdominal wall recurrence after open colectomy was considered to be rare–~0.7% according to a retrospective study by Hughes et al. [127]. However, Cass et al. reported abdominal wall recurrence in 2.5% of patients after open resection of coloncancer [128], and Gunderson et al. showed that two-thirds of abdominal wall recurrences are missed by physical examination of the abdominal wall [129]. At second-look laparotomy 3 months after the open curative resection of coloncancer, 3.3% of patients suffered a recurrence in the abdominal wall.

In the literature on laparoscopic resection of coloncancer published before 1995, high incidences of port site metastasis were reported, ranging from 0.6% to 21% [130–133]. In a review of data from reports on laparoscopic resection of coloncancer published later, a much lower rate of 0.85% was recorded in an analysis of 1,769 operation [23]. Wittich et al. analyzed data from 16

Table 15. Case reports on port site metastasis

Study	Year	Duke's stage	Months to recurrence
Alexander [171]	1993	C	3
O'Rourke [172]	1993	B	10
Walsh [173]	1993	C	6
Fusco [174]	1993	C	10
Cirocco [175]	1994	C	9
Nduka [176]	1994	C	3
Prasad [176]	1994	B	6
		A	26
Berends [130]	1994	B	NA
		C	NA
		D	NA
Lauroy [177]	1994	A	9
Ramos [178]	1994	C	NA
		C	NA
		C	NA
Cohen [179]	1994	B	3
		B	6
		C	6
		C	9
		C	12
Jacquet [180]	1995	B	10
		B	9
Montorsi [25]	1995	B	2

NA, not available

Table 16. Measurements of plasma interleukin-6 (IL-6) levels (in pg/ml)

Study	Preoperative	Laparoscopic	Open	*p* Value
1–2				
Ordemann [142]	NA	Significantly lower after laparoscopy		< 0.01
Schwenk [144]	4.25 (3.4–7.7)	34.0 (25.6–48.7)	50.5 (39.8–75.7)	0.03
Hewitt [102]	NA	173 ± 156	313 ± 294	0.25
Wu [145]	NA	83 ± 7	105 ± 33	< 0.05
3				
Sietses [146]	1.75 ± 1.64	85.6 ± 82.3	132.1 ± 143.8	NS
Fukushima [150]	NA	Significantly higher after laparoscopy		< 0.05
Delgado [149]	NA	239.5 (49.1–645.7)	372.7 (31.4–3.226)	< 0.05
Nishiguchi [147]	NA	Significantly lower after laparoscopy		< 0.05

NS, not significant; NA, not available
Results given as mean ± SD or median (range)

Table 17. Measurements of plasma C-reactive protein (CRP) (in mg/dl)

Study	Preoperative	Laparoscopic	Open	*p* value
1–2				
Schwenk [144]	NA	40 (33.0–49.4)	61.2 (52.0–77.9)	0.002
Wu [145]	6.4	NA	NA	NS
3				
Fukushima [150]	NA	NA	NA	NS
Delgado [149]	NA	6.9 ± 4.5	9.1 ± 4.8	0.01
Nishiguchi [147]	NA	Significantly lower after laparoscopy		0.05

NA, not available; NS, not significant
Results given as mean ± SD or mean (range)

studies, including a total of 3,547 patients, 30 of whom (0.85%) developed port site metastases [134]. In a recent systematic review, 11 port site metastases were found in 1,114 operations, translating to an incidence of 1% [96]. The high incidences of port site metastasis in early reports on laparoscopic surgery appear to reflect inexperience with the technique, such that an oncologically appropriate operation was not performed. The details of the published port site metastases are shown in Tables 14 and 15.

Statement 23: Port site metastasis

The incidence of port site metastases after laparoscopic colectomy is < 1% (Level of evidence: 2c).

Quality of life

Health-related quality of life associated with laparoscopic colon resection for malignancy has been addressed only by Weeks et al. [115]. The investigators used the Symptoms Distress Scale, Quality of Life Index (QLI), and a global rating scale. The only statistically significant difference reported was the global rating scale score 2 weeks postoperatively ($p = 0.009$). In this study, both the global rating scale and the QLI were not employed during the first 2 postoperative weeks, despite the probability that differences in quality of life are likely to be most evident and most pronounced in the early days after surgery.

Costs

The issue of costs associated with the implementation of health care technologies is of increasing importance. Not only are financial demands on health care increasing, but at the same time health budgets are limited. Currently, there are no prospective cost-effectiveness evaluations available for laparoscopic colon resection. Some evaluations are currently being conducted alongside large multicenter RCT. In the CLASICC [123], COST [124], and COLOR [125] trials, cost-effectiveness of the two approaches is being evaluated. Such analyses include both direct costs (costs primarily associated with treatment) and indirect costs (costs secondarily related to disease or treatment).

Direct costs

In-hospital costs need to be carefully evaluated. In a retrospective review, the in-hospital costs of laparoscopically assisted right hemicolectomy were compared to the costs of open colectomy [135]. Costs were collected only from the time of operation until the time of discharge and thus reflected only hospital costs. This study reported higher direct costs for laparoscopic hemicolectomy than for open hemicolectomy due to increased operating time and the use of disposables (ADD 9,064 vs AUD 7,881, respectively). A review of the hospital costs of laparoscopic colectomy concluded that the shorter hospital stay in the laparoscopy arm more than compensated for the increased operating room costs, resulting in lower total hospital costs for laparoscopic colectomy (USD 9,811 vs USD 11,207) [136]. This evaluation included operations for both benign and malignant disease of the colon. In a prospective study, direct in-hospital costs for laparoscopic colectomy were also lower than those for open surgery (DM 5,400 vs DM 7,500) [113]. However, this large study included operations for both benign and malignant colorectal disease and violated the intention-to-treat principle.

Table 18. Summary of all statements and recommendations

	No.	Statements and recommendations	Level of evidence	Grade of recommendation
Preoperative evaluation and selection of patients				
Recommendation	1	Preoperative imaging studies of colon cancer to assess the size of the tumor, possible invasion of adjacent structures, and localization of the tumor are recommended in laparoscopic surgery for colon cancer.	5	Grade D
Statement	2	Age only is not a contraindication for laparoscopic resection of colon cancer.	2b	—
Recommendation	3	Invasive monitoring of blood pressure and blood gases is mandatory in ASA II–CPôIV patients (no consensus: 91% agreement among experts).		Grade A
		Low-pressure (< 12 mmHg) pneumoperitoneum is advocated in ASA II–IV patients.		Grade B
Statement	4	Obesity is not an absolute contraindication, but the rates of complications and conversions are higher at BMI > 30 (no consensus: 93% agreement among experts).	2c	—
Recommendation	5	Potentially curative resections of colonic cancer suspected of invading the abdominal wall or adjacent structures should be undertaken by open surgery (no consensus: 83% agreement among experts).	5	Grade D
Statement	6	Adhesions do not appear to be a contraindication to laparoscopic colectomy.	4	—
Operative technique				
Statement	7	Placement of trocars is based on the experience and the preference of the individual surgeon.	5	—
Recommendation	8	High-quality videoscopic imaging is strongly recommended.	5	Grade D
Statement	9	Proper surgical technique and practice reduces the likelihood of port site metastasis.	5	—
Recommendation	10	Preoperative tattooing of small colon tumors is advised. The alternatives are intraoperative colonoscopy or preoperative colonoscopic clipping followed by peroperative fluoroscopy or ultrasonography.	5	Grade D
Recommendation	11	Dissection of the mesocolon from medial to lateral is the preferred approach in laparoscopic colonic surgery.	5	Grade D
		Intraoperative results of laparoscopic resection of colon cancer		
Statement	12	Laparoscopic colectomy is converted to open surgery in 14% of cases (0—42%). The most common causes of conversion are tumor invasion of adjacent structures or bulky tumor, adhesions, and technical failure.	3a	—
Statement	13	Laparoscopic colectomy requires more operating time than open colectomy.	2a	—
Statement	14	The extent of laparoscopic lymphadenectomy and bowel resection is similar to those obtained by open colectomy.	2b	—
Clinical outcome				
Statement	15	Morbidity after laparoscopic colectomy does not differ from that after open colectomy.	2b	—
Statement	16	Mortality of laparoscopic colectomy appears to be similar to that of open colectomy.	2b	—
Statement	17	Hospital stay is shorter after laparoscopic resection of colon cancer than after open colectomy.	1a	—
Statement	18	Pain is less severe after laparoscopic colectomy.	2a	—
Statement	19	Less analgesia is needed after laparoscopic colectomy compared to open colectomy.	1b	—
Statement	20	Gastrointestinal function recovers earlier after laparoscopic colectomy.	2b	—
Statement	21	Postoperative pulmonary function is less impaired after laparoscopic is open resection of colon cancer.	1b	—
Statement	22	Cancer-related survival after laparoscopic resection appears to be at least equal to open resection.	2a	—
Statement	23	The incidence of port site metastases after laparoscopic colectomy is < 1%.	2c	—
Costs				
Statement	24	The operative costs for the laparoscopic resection of colon cancer are higher because of a longer operating time and the use of more expensive (disposable) devices.	3b	—
Postoperative stress response				
Statement	25	Stress response after laparoscopic colectomy is lower.	1b	—

BMI, body mass index

Out-of-hospital costs

Out-of-hospital costs, such as visits to outpatient clinics, home care, and visits to family doctors, have not yet been estimated for laparoscopic colectomy.

Indirect costs

The preferred method of cost analysis is to evaluate cost-effectiveness from a societal perspective. This implies the measurement of indirect costs. The most important indirect costs are incurred from patients who are employed but are unable to work, causing loss of productivity. One might argue that a faster recovery would lead to patients returning to work earlier. Koehler et al. reported that such costs were lower for laparoscopic colectomy (DM 1,600) than for open colectomy (DM 2,200).

Cost-effectiveness

For policy making and the implementation of new techniques, one must assess both the costs associated with this technique as well as the effects of this technique and its widespread safe applicability. Survival is the most important endpoint after the resection of coloncancer. The differences in costs between laparoscopic and open colorectal surgery have to be assessed in the context of survival rates obtained by the two approaches. The next endpoint in order of importance is quality of life. The calculation of quality-adjusted life years combines both. No cost-effectiveness studies have been reported.

Statement 24: Costs

The operative costs for the laparoscopic resection of coloncancer are higher because of a longer operating time and the use of more expensive (disposable) devices. (Level of evidence: 3b).

Postoperative stress response

Stress response after laparoscopy

Laparoscopic surgery induces less trauma than conventional surgery and is thus likely to depress the immune response to a lesser extent. The preservation of the peritoneal and systemic immune system is important to prevent infections, sepsis, and the implantation of tumor cells to the traumatized tissues. In general, open surgery appears to inflict a greater nonspecific depression of the immune response than the laparoscopic approach.

Carbon dioxide pneumoperitoneum may impair the local immunity of the peritoneal lining. Peritoneal macrophages produce less cytokines [31, 32], and their intrinsic function (phagocytosis) [137, 138] diminishes on exposure to carbon dioxide insufflation.

Systemic immunity is depressed to a lesser extent by laparoscopic surgery than conventional open surgery. Both experimental and clinical studies on delayed-type hypersensitivity (DTH) response [139, 140], production of cytokines [141], and expression of HLA-DR receptors [139, 142] have confirmed this.

Stress response during colectomy

It has been suggested that survival may be improved if immunosupression induced by surgery could be reduced or eliminated [143]. The acute-phase response is a good index of the immune status of patients. Production of acute-phase proteins by hepatocytes often increases a thousandfold, as does C-reactive protein (CRP) after tissue injury. This reaction of liver cells is induced by corticoids and cytokines, of which interleukin-6 (IL-6) is the main activator. During recovery, the levels of acute-phase proteins normalize. This acute-phase reaction has been measured in most studies by monitoring the levels of IL-6 and CRP (Tables 16 and 17).

Most studies demonstrated lower IL-6 levels after laparoscopic colorectal resection compared with open conventional surgery [102, 142, 144–149]. Only one study reported a significant raise in IL-6 serum level after laparoscopic sigmoidectomy [150]. Although IL-6 was lower after laparoscopic colectomy, studies have shown conflicting CRP data (see Table 17).

In addition to cytokines, other cell-related parameters, such as DTH and CD4/CD8 markers, have been assessed after laparoscopic colectomy, with no significant changes reported between laparoscopic and open colorectal surgery [102, 151].

Statement 25: Stress response

Stress response after laparoscopic colectomy is lower (Level of evidence: 1b).

References

1. Hilliard G, et al. (1990) The elusion colonic malignancy: a need for definitive preoperative localization. Am Surg 56: 742–744
2. Ott DJ (2000) Accuracy of doublecontrast barium enema in diagnosing colorectal polyps and cancer. Semin Roentgenol 35: 333–341
3. Pijl ME, et al. (2002) Radiology Colorectal cancer. Eur J Cancer 38: 887–898
4. Bond JH (2002) Colorectal cancer screening: the potential role of virtual colonoscopy. J Gastroenterol 37(Suppl 13): 92–96
5. Delgado S, et al. (2000) Could age be an indication for laparoscopic colectomy in colorectal cancer? Surg Endosc 14: 22–26
6. Schwandner O, Schiedeck TH, Bruch HP (1999) Advanced age–indication or contraindication for laparoscopic colorectal surgery? Dis Colon Rectum 42: 356–362
7. Lo CM, et al. (1996) Laparoscopic cholecystectomy for acute cholecystitis in the elderly. World J Surg 20: 983–986; discussion 987
8. Pessaux P, et al. (2000) Laparoscopic cholecystectomy in the elderly: a prospective study. Surg Endosc 14: 1067–1069
9. Neudecker J, et al. (2002) The EAES clinical practice guideline on the pneumoperitoneum for laparoscopic surgery. Surg Endosc 16: 1121–1143
10. Sprung J, et al. (2002) The impact of morbid obesity, pneumoperitoneum, and posture on respiratory system mechanics and oxygenation during laparoscopy. Anesth Analg 94: 1345–1350

11. Pandya S, et al. (1999) Laparoscopic colectomy: indications for conversion to laparotomy. Arch Surg 134: 471–475
12. Pikarsky AJ, et al. (2002) Is obesity a high risk factor for laparoscopic colorectal surgery? Surg Endosc 16: 855–858
13. Angrisani L, et al. (1995) Laparoscopic cholecyslectomy in obese patients compared with nonobese patients. Surg Laparosc Endosc 5: 197–201
14. Collet D, et al. (1992) Laparoscopic cholecystectomy in the obese patient. Surg Endosc 6: 186–188
15. Miles RH, et al. (1992) Laparoscopy: the preferred method of cholecystectomy in the morbidly obese. Surgery 112: 818–822; discussion 822–823
16. Phillips EH, et al. (1994) Comparison or laparoscopic cholecystectomy in obese and non-obese patients. Am Surg 60: 316–321
17. Schirmer BD, et al. (1992) Laparoscopic cholecystectomy in the obese patient. Ann Surg 216: 146–152
18. Unger SW, et al. (1991) Laparoscopic approach to gallstones in the morbidly obese patient. Surg Endosc 5: 116–117
19. Nelson H, et al. (2001) Guidelines 2000 for colon and rectal cancer surgery. J Natl Cancer Inst 93: 583–596
20. Hamel CT, et al. (2000) Do prior abdominal operations after the outcome of laparoscopically assisted right hemicolectomy? Surg Endosc 14: 853–857
21. Boulanger A, Hardy JF (1987) [Intestinal distention during elective abdominal surgery: should nitrous oxide be banished?]. Can J Anaesth 34: 346–350
22. Taylor E, et al. (1992) Anesthesia for laparoscopic cholecystectomy: is nitrous oxide contraindicated? Anesthesiology 76: 541–543
23. Zmora O, Weiss EG (2001) Trocar site recurrence in laparoscopic surgery for colorectal cancer: myth or real concern? Surg Oncol Clin North Am 10: 625–638
24. Bouvy ND, et al. (1996) Impact of gas(less) laparoscopy and laparotomy on peritoneal tumor growth and abdominal wall metastases. Ann Surg 224: 694–700; discussion 700–701
25. Montorsi M, et al. (1995) Early parietal recurrence of adenocarcinoma of the colon after laparoscopic colectomy. Br J Surg 82: 1036–1037
26. Watson DI, et al. (1997) Gasless laparoscopy may reduce the risk of port-site metastases following laparaccopic tumor surgery. Arch Surg 132: 166–168; discussion 169
27. Gutt CN, et al. (1999) Impact of laparoscopic colonic resection on tumour growth and spread in an experimental model. Br J Surg 86: 1180–1184
28. Iwanaka T, Arya G, Ziegler MM (1998) Mechanism and prevention of port-site tumor recurrence after laparoscopy in a murine model. J Pediatr Surg 33: 457–461
29. Wittich P, et al. (2000) Intraperitoneal tumor growth is influenced by pressure of carbon dioxide pneumoperitoneum. Surg Endosc 14: 817–819
30. Gutt CN, et al. (1997) The phagocytisis activity during conventional and laparoscopic operations in the rat: a preliminary study. Surg Endosc 11: 899–901
31. West MA, Baker J, Bellingham J (1996) Kinetics of decreased LPS-stimulated cytokine release by macrophages exposed to CO2. J Surg Res 63: 269–274
32. Hajri A, et al. (2000) Dual effect of laparoscopy on cell-mediated immunity. Eur Surg Res 325: 261–6
33. Jacobi CA, et al. (2001) The impact of conventional and laparoscopic colon resection (CO2 or helium) on intraperitoneal adhesion formation in a rat peritonitis model. Surg Endosc 15: 380–386
34. Nagelschmidt M, Gerbecks D, Minor T (2001) The impact of gas laparoscopy on abdominal plasminogen activator activity. Surg Endosc 15: 585–588
35. Neuhaus SJ, et al. (1998) Tumor implantation following laparoscopy using different insufflation gases. Surg Endosc 12: 1300–1302
36. Jacobi CA, et al. (1999) Influence of different gases and intraperitoneal instillation of antiadherent or cytotoxic agents on peritoneal tumor cell growth and implantation with laparoscopic surgery in a rat model. Surg Endosc 13: 1021–1025
37. Bouvy ND, et al. (1998) Effects of carbon dioxide pneumoperitoneum, air pneumoperitoneum, and gasless laparoscopy on body weight and tumor growth. Arch Surg 133: 652–656
38. Wu JS, et al. (1998) Excision of trocar sites reduces tumor implantation in an animal model. Dis Colon Rectum 41: 1107–1111
39. Watson DI, et al. (2002) Excision of laparoscopic port sites increases the likelyhood of wound metastases in an experimental model. 8th World Congress of Endoscopic Surgery, New York, NY, USA. BS01(final program) pp 77
40. Neuhaus SJ, et al. (1999) Influence of cytotoxic agents on intraperitoneal tumor implantation after laparoscopy. Dis Colon Rectum 42: 10–15
41. Lee SW, et al. (1999) Peritoneal irrigation with povidone-iodine solution after laparoscopic-assisted splenectomy significantly decreases port-tumor recurrence in a murine model. Dis Colon Rectum 42: 319–326
42. Neuhaus SJ, et al. (1999) Experimental study of the effect of intraperitoneal heparin on tumour implantation following laparoscopy. Br J Surg 86: 400–404
43. Braumann C, et al. (2000) influence of intraperitoneal and systemic application of taurolidine and taurolidine/heparin during laparoscopy on intraperitoneal and subcutaneous tumour growth in rats. Clin J Exp Metastasis 18: 547–552
44. Jacobi CA, et al. (1999) New therapeutic strategies to avoid intra- and extraperitoneal metastases during laparoscopy: results of a tumor model in the rat. Dig Surg 16: 393–399
45. Eshraghi N, et al. (1999) Topical treatments of laparoscpoic port sites can decrease the incidence of incision metastasis. Surg Endosc 13: 1121–1124
46. Tseng LN, et al. (1998) Port-site metastases: impact of local tissue trauma and gas leakage. Surg Endosc 12: 1377–1380
47. Wittich P, et al. (2000) Port-site metastases after CO(2) laparoscopy: is aerosolization of tumor cells a pivotal factor? Surg Endosc 14: 189–192
48. Whelan RL, et al. (1996) Trocar site recurrence is unlikely to result from aerosolization of tumor cells. Dis Colon Rectum 39(10 Suppl): S7–S13
49. Turnbull RB Jr, et al. (1967) Cancer of the colon: the influence of the no-touch isolation technique on survival rates. Ann Surg 166: 420–427
50. Wiggers T, et al. (1988) No-touch isolation technique in colon cancer: a controlled prospective trial. Br J Surg 75: 409–415
51. Gertsch P, et al. (1992) Malignant cells are collected on circular staplers. Dis Colon Rectum 35: 238–241
52. Fermor B, et al. (1986) Proliferative and metastatic potential of exfoliated colorectal cancer cells. J Natl Cancer Inst 76: 347–349
53. Umpleby HC, et al. (1984) Viability of exfoliated colorectal carcinoma cells. Br J Surg 71: 659–663
54. Jenner DC, et al. (1998) Rectal washout eliminates exfoliated malignant cells. Dis Colon Rectum 41: 1432–1434
55. McDermott JP, Devereaux DA, Caushaj PF (1994) Pitfall of laparoscopic colectomy: an unrecognized synchronous cancer. Dis Colon Rectum 37: 602–603
56. Larach SW, et al. (1997) Complications of laparoscopic colorectal surgery: analysis and comparison of early vs latter experience. Dis Colon Rectum 40: 592–596
57. Lacy AM, et al. (1995) Is laparoscopic colectomy a safe procedure in synchronous colorectal carcinoma? Report of a Case. Surg Laparosc Endosc 5: 75–76
58. Tabibian N, et al. (1988) Use of an endoscopically placed clip can avoid diagnostic errors in colonoscopy. Gastrointest Endosc 34: 262–264
59. Ohdaira T, et al. (1999) Intraoperative localization of colorectal tumors in the early stages using a marking clip detector system. Dis Colon Rectum 42: 1353–1355
60. Hammond DC, et al. (1989) Endoscopic tattooing of the colon: an experimental study. Am Surg 55: 457–461
61. Botoman VA, Pietro M, Thirlby RC (1994) Localization of colonic lesions with endoscopic tattoo. Dis Colon Rectum 37: 775–776
62. Waye JD (1992) Mucosal marking of the colon, or india ink tattoo of the colon: advanced therapeutic endoscopy. 2nd ed. Raven Press, New York, pp 209–214
63. Coman E, et al. (1991) Fat necrosis and inflammatory pseudotumor due to endoscopic tattooing of the colon with india ink. Gastrointest Endosc 37: 65–68

64. Montorsi M, et al. (1999) Original technique for small colorectal tumor localization during laparoscopic surgery. Dis Colon Rectum 42: 819–822
65. Cohen JL, Forde KA (1988) Intraoperative colonoscopy. Ann Surg 207: 231–233
66. Fu KII, et al. (2001) A new endosocopic tattooing technique for identifying the location of colonic lesions during laparoscopic surgery: a comparison with the conventional technique. Endoscopy 33: 687–691
67. Nizam R, et al. (1996) Colonic tattooing with India ink: benefits, risks, and alternatives. Am J Gastroenterol 91: 1804–1808
68. Park SI, et al. (1991) Colonic abscess and focal peritonities secondary to india ink tattooing of the colon. Gastrointest Endosc 37: 68–71
69. Bernstein MA, et al. (1996) Is complete laparoscopic colectomy superior to laparoscopic assisted colectomy? Am Surg 62: 507–511
70. Kurian MS, et al. (2001) Hand-assisted laparoscopic surgery: an emerging technique. Surg Endosc 15: 1277–1281
71. Bemelman WA, et al. (1996) Laparoscopic-assisted colectomy with the dexterity pneumo sleeve. Dis Colon Rectum 39(10 Suppl): S59–S61
72. Simons AJ, et al. (1995) Laparoscopic-assisted colectomy learning curve. Dis Colon Rectum 38: 600–603
73. Schlachta CM, et al. (2001) Defining a learning curve for laparoscopic colorectal resections. Dis Colon Rectum 44: 217–222
74. Bennett CL, et al. (1997) The learning curve for laparoscopic colorectal surgery: preliminary results from a prospective analysis of 1194 laparoscopic-assisted colectomies. Arch Surg 132: 41–44; discussion 45
75. Lezoche E, et al. (2000) Laparoscopic colonic resections versus open surgery: a prospective non-randomized study on 310 unselected cases. Hepatogastroenterology 47: 697–708
76. Kwok SP, et al. (1996) Prospective evaluation of laparoscopic-assisted large bowel excision for cancer. Ann Surg 223: 170–176
77. Milsom JW, et al. (1998) A prospective, randomized trial comparing laparoscopic versus conventional techniques in colorectal cancer surgery: a preliminary report. J Am Coll Surg 187: 46–54; discussion 54–55
78. Falk PM, et al. (1993) Laparoscopic colectomy: a critical appraisal. Dis Colon Rectum 36: 28–34
79. Dean PA, et al. (1994) Laparoscopic-assisted segmental colectomy: early Mayo Clinic experience. Mayo Clinic Proc 69: 834–840
80. Huscher C, et al. (1996) Laparoscopic colorectal resection: a multicenter Italian study. Surg Endosc 10: 875–879
81. Lauter DM, Froines EJ (2001) Initial experience with 150 cases of laparoscopic assisted colectomy. Am J Surg 181: 398–403
82. Lumley JW, et al. (1996) Laparoscopic-assisted colorectal surgery: lessons learned from 240 consecutive patients. Dis Colon Rectum 39: 155–159
83. Phillips EH, et al. (1992) Laparoscopic colectomy. Ann Surg 216: 703–707
84. Lezoche E, et al. (2002) Laparoscopic vs open hemicolectomy for colon cancer. Surg Endosc 16: 596–602
85. Marusch F, et al. (2001) Experience as a factor influencing the indications for laparoscopic colorectal surgery and the results. Surg Endosc 15: 116–120
86. Fielding GA, et al. (1994) Laparoscopic colectomy. Surg Endosc 11: 745–749
87. Curet MJ, et al. (2000) Laparoscopically assisted colon resection for colon carcinoma: perioperative results and long-term outcome. Surg Endosc 14: 1062–1066
88. Bouvet M, et al. (1998) Clinical, pathologic, and economic parameters of laparoscopic colon resection for cancer. Am J Surg 176: 554–558
89. Lacy AM, et al. (2002) Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. Lancet 359: 2224–2229
90. Khalili TM, et al. (1998) Colorectal cancer: comparison of laparoscopic with open approaches. Dis Colon Rectum 41: 832–838
91. Marubashi S, et al. (2000) The usefulness, indications, and complications of laparoscopy-assisted colectomy in comparison with those of open colectomy for colorectal carcinoma. Surg Today 30: 491–496
92. Leung KL, et al. (1997) Laparoscopic-assisted resection of rectosigmoid carcinoma: immediate and medium-term results. Arch Surg 132: 761–764; discussion 765
93. Lacy AM, et al. (1995) Short-term outcome analysis of a randomized study comparing laparoscopic vs open coloctomy for colon cancer. Surg Endosc 9: 1101–1105
94. Stage JG, et al. (1997) Prospective randomized study of laparoscopic verus open colonic resection for adenocarcinoma. Br J Surg. 84: 391–396
95. Bokey EL, et al. (1996) Morbidity and mortality following laparoscopic-assisted right hemicolectomy for cancer. Dis Colon Rectum: 39(10 Suppl): S24–S28
96. Chapman AE, et al. (2001) Laparoscopic assisted resection of colorectal malignancies a systematic review. Ann Surg 234: 590–606
97. Wexner SD, et al. (1993) Laparoscopic colorectal surgery: a prospective assessment and current perspective. Br J Surg 80: 1602–1605
98. Lord SA, et al. (1996) Laparoscopic resections for colorectal carcinoma: a three-year experience. Dis Colon Rectum 39: 148–154
99. Van Ye TM, Cattey RP, Henry LG (1994) Laparoscopically assisted colon resections compare favorably with open technique. Surg Laparosc Endosc: 4: 25–31
100. Bonjer HJ, et al. (1997) Open versus closed establishment of pneumoperitoneum in laparoscopic surgery. Br J Surg 84: 599–602
101. Winslow ER, et al. (2002) Wound complication of laparoscopic vs open colectomy. 8th World Congress of Endoscopic Surgery, New York, NY, USA. Final program (S183): 120
102. Hewitt PM, et al. (1998) Laparoscopic-assisted vs. open surgery for colerectal cancer: comparative study of immune effects. Dis Colon Rectum 41: 901–909
103. Bokey EL, et al. (1997) Laparoscopic resection of the colon and rectum for cancer. Br J Surg. 84: 822–825
104. Leung KL, et al. (1999) Laparoscopic-assisted resection of right-sided colonic carcinoma: a case-control study. J Surg Oncol 71: 97–100
105. Goh YC, Eu KW, Seow-Choen F (1997) Early postoperative results of a prospective series of laparoscopic vs. open anterior resections for rectosigmoid cancers. Dis Colon Rectum 40: 776–780
106. Tate JJ, et al. (1993) Propective comparison of laparoscopic and conventional anterior resection. Br J Surg. 80: 1396–1398
107. Delgado Gomis F, et al. (1998) Early results of laparoscopic resection of colorectal cancer. Rev Esp Enferm Dig 90: 323–334
108. Leung KL, et al. (1999) Laparoscopic-assisted resection of colorectal carcinoma: five-year audit. Dis Colon Rectum 42: 327–332discussion 332–333
109. Vara-Thorbeck C, et al. (1994) Indications and advantages of laparoscopy-assisted colon resection for carcinoma in elderly patients. Surg Laparosc Endosc 4: 110–118
110. Lacy AM, et al. (1998) Port site metastases, and recurrence after laparoscopic colectomy: a randomized trial. Surg Endosc 12: 1039–1042
111. Schwenk W, et al. (1999) Pulmonary function following laparoscopic or conventional colorectal resection: a randomized controlled evaluation. Arch Surg 134: 6–12; discussion 13
112. Hong D, Tabet J, Anvari M (2001) Laparoscopic vs. open resection for colorectal adenocarcinoma. Dis Colon Rectum 44: 10–18; discussion 18–19
113. Kohler L, Holthausen U, Troidl H (1997) [Laparoscopic colorectal surgery–attempt at evaluating a new technology]. Chirurg 68: 794–800; discussion 800
114. Santoro E, et al. (1999) Colorectal carcinoma: laparoscopic versus traditional open surgery. A clinical trial. Hepatogastroenterology 46: 900–904
115. Weeks JC, et al. (2002) Short-term quality-of-life outcomes following laparoscopic-assisted colectomy vs open colectomy for colon cancer: a randomized trial. JAMA 287: 321–328
116. Franklin ME Jr, et al. (1996) Prospective comparison of open vs. laparoscopic colon surgery for carcinoma: five-year results. Dis Colon Rectum 39(10 Suppl): S35–S46
117. Psaila J, et al. (1998) Outcome following laparoscopic resection for colorectal cancer. Br J Surg 85: 662–664

118. Franklin ME Jr, Rosenthal D, Norem RF (1995) Prospective evaluation of laparoscopic colon resection versus open colon resection for adenocarcinoma: a multicenter study. Surg Endosc 9: 811–816
119. Wilmore DW, Kehlet H (2001) Management of patients in fast track surgery. BMJ 322: 473–476
120. Schwenk W, Bohm B, Muller JM (1998) Postoperative pain and fatigue after laparoscopic or conventional colorectal resections: a prospective randomized trial. Surg Endosc 12: 1131–1136
121. Hardacre JM, Talamini MA (2000) Pulmonary and hemodynamic changes during laparoscopy–are they important? Surgery 127: 241–244
122. Milsom JW, et al. (1994) Use of laparoscopic techniques in colorectal surgery: preliminary study. Dis Colon Rectum 37: 215–218
123. Stead ML, et al. (2000) Assessing the relative costs of standard open surgery and laparoscopic surgery in colorectal cancer in a randomised controlled trial in the United Kingdom. Crit Rev Oncol Hematol 33: 99–103
124. Nelson H, Weeks JC, Wieand HS (1995) Proposed phase III trial comparing laparoscopic-assisted colectomy versus open colectomy for colon cancer. J Natl Cancer Inst Monogr 19: 51–56
125. Anonymous (2000) COLOR: Dig Surg 17: 617–622
126. Feliciotti F, et al. (2002) Results of laparoscopic vs open resections for colon cancer in patients with a minimum follow-up of 3 years. Surg Endosc 16: 1158–1161
127. Hughes ES, et al. (1983) Tumor recurrence in the abdominal wall scar tissue after large-bowel cancer surgery. Dis Colon Rectum 26: 571–572
128. Cass AW, Million RR, Pfaff WW (1976) Patterns of recurrence following surgery alone for adenocarcinoma of the colon and rectum. Cancer 37: 2861–2865
129. Gunderson LL, Sosin H (1974) Areas of failure found at reoperation (second or symptomatic look) following "curative surgery" for adenocarcinoma of the rectum: clinicopathologic correlation and implications for adjuvant therapy. Cancer 34: 1278–1292
130. Berends FJ, et al. (1994) Subcutaneous metastases after laparoscopic colectomy. Lancet 344: 58
131. Ortega AE, et al. (1995) Laparoscopic Bowel Surgery Registry: preliminary results. Dis Colon Rectum. 38: 681–685; discussion 685–686
132. Wexner SD, et al. (1995) Laparoscopic colorectal surgery–are we being honest with our patients? Dis Colon Rectum 38: 723–727
133. Wexner SD, Cohen SM (1995) Port site metastases after laparoscopic colorectal surgery for cure of malignancy. Br J Surg 82: 295–298
134. Wittich P, Bonjer HJ (2000) Port-site recurrences in laparoscopic surgery. In: Kockerling F (Port-site and wound recurrences in cancer surgery. Heidelberg, Springer-Verlag, pp 12–20
135. Philipson BM, et al. (1997) Cost of open versus laparoscopically assisted right hemicolectomy for cancer. World J Surg 21: 214–217
136. Musser DJ, et al. (1994) Laparoscopic colectomy: at what cost? Surg Laparosc Endosc 4: 1–5
137. Gutt CN, et al. (1997) The phagocytosis activity during conventional and laparoscopic operations in the rat: a preliminary study. Surg Endosoc 11: 899–901
138. Chekan EG, et al. (1999) Intraperitoneal immunity and pneumoperitoneum. Surg Endosc 13: 1135–1138
139. Kloosterman T, et al. (1994) Unimpaired immune functions after laparoscopic cholecystectomy. Surgery 115: 424–428
140. Schietroma M, et al. (2001) Evaluation of immune response in patients after open or laparoscopic cholecystectomy. Hepatogastroenterology 48: 642–646
141. Liang JT, et al. (2002) Prospective evaluation of laparoscopy-assisted colectomy versus laparotomy with resection for management of complex polyps of the sigmoid colon. World J Surg 26: 377–383
142. Ordemann J, et al. (2001) Cellular and humoral inflammatory response after laparoscopic and conventional colorectal resections. Surg Endosc 15: 600–608
143. Eggermont AM, Steller EP, Sugarbaker PH (1987) Laparotomy enhances intraperitoneal tumor growth and abrogates the anti-tumor effects of interleukin-2 and lymphokine-activated killer cells. Surgery 102: 71–78
144. Schwenk W, et al. (2000) Inflammatory response after laparoscopic and conventional colorectal resections–results of a prospective randomized trial. Langenbecks Arch Surg 385: 2–9
145. Wu FPK, et al. (2003) Systemic and peritoneal inflammatory response after a laparoscopic or conventional colon resection in cancer patients: a prospective, randomized trial. Dis Colon Rectum 46: 147–155
146. Sietses C, et al. (2000) Laparoscopic surgery preserves monocyte-mediated tumor cell killing in contrast to the conventional approach. Surg Endosc 14: 456–460
147. Nishiguchi K, et al. (2001) Comparative evaluation of surgical stress of laparoscopic and open surgeries for colorectal carcinoma. Dis Colon Rectum 44: 223–230
148. Kuntz C, et al. (2000) Short- and long-term results after laparoscopic vs conventional colon resection in a tumor-bearing small animal model. Surg Endosc 14: 561–567
149. Delgado S, et al. (2001) Acute phase response in laparoscopic and open colectomy in colon cancer: randomized study. Dis Colon Rectum 44: 638–646
150. Fukushima R, et al. (1996) Interleukin-6 and stress hormone responses after uncomplicated gasless laparoscopic-assisted and open sigmoid colectomy. Dis Colon Rectum 39(10 Suppl): S29–S34
151. Tang CL, et al. (2001) Randomized clinical trial of the effect of open versus laparoscopically assisted colectomy on systemic immunity in patients with colorectal cancer. Br J Surg 88: 801–807
152. Schiedeck TH, et al. (2000) Laparoscopic surgery for the cure of colorectal cancer: results of a German five-center study. Dis Colon Rectum 43: 1–8
153. Millikan KW, et al. (1996) Superior mesenteric and portal vein thrombosis following laparoscopic-assisted right hemicolectomy: report of a case. Dis Colon Rectum 39: 1171–1175
154. Franklin ME, et al. (2000) Laparoscopic surgery for stage III colon cancer: long-term follow-up. Surg Endosc 14: 612–616
155. Poulin EC, et al. (1999) Laparoscopic resection does not adversely affect early survival curves in patients undergoing surgery for colorectal adenocarcinoma. Ann Surg 229: 487–492
156. Schwenk W, et al. (1998) Laparoscopic versus conventional colorectal resection: a prospective randomised study of postoperative ileus and early postoperative feeding. Langenbecks Arch Surg 383: 49–55
157. Delgado F, et al. (1999) Laparoscopic colorectal cancer resection: initial follow-up results. Surg Laparosc Endosc Percutan Tech 9: 91–98
158. Cook TA, Dehn TC (1996) Port-site metastases in patients undergoing laparoscopy for gastrointestinal malignancy. Br J Surg 83: 1419–1420
159. Hoffman GC, et al. (1996) Minimally invasive surgery for colorectal cancer: initial follow-up. Ann Surg 223: 790–796, discussion 796798
160. Molenaar CB, Bijnen AB, de Ruiter P (1998) Indications for laparoscopic colorectal surgery. results from the Medical Centre Alkmaar, The Netherlands. Surg Endosc 12: 42–45
161. Quattlebaum JK Jr, Flanders HD, Usher CH (1993) Laparoscopically assisted colectomy. Surg Laparosc Endosc 3: 81–87
162. Ballantyne GH (1995) Laparoscopic-assisted colorectal surgery: review of results in 752 patients. Gastroenterologist 3: 75–89
163. Fleshman JW, et al. (1996) 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 39(10 Suppl): S53–S58
164. Rosato P, et al. (1998) Port-site and wound metastases following laparoscopic resection of colorectal carcinoma: the experience of the Italian registry. Presented at the 33rd Congress of the European Society for Surgical Research (ESSR)
165. Vukasin P, et al. (1996) Wound recurrence following laparoscopic colon cancer resection: results of the American Society of Colon and Rectal Surgeons Laparoscopic Registry. Dis Colon Rectum 39(10 Suppl): S20–S23
166. Gellman L, Salky B, Edye M (1996) Laparoscopic assisted colectomy. Surg Endosc 10: 1041–1044
167. Kok KY, et al. (1996) Laparoscopic-assisted large bowel resection. Ann Acad Med Singapore 25: 650–652

168. Guillou PJ, Darzi A, Monson JR (1993) Experience with laparoscopic colorectal surgery for malignant disease. Surg Oncol 2(Suppl 1): 43–49
169. Croce E, et al. (1997) Laparoscopic colectomy: the absolute need for a standard operative technique. Jsls 1: 217–224
170. Kawamura YJ, et al. (1995) Laparoscopic-assisted colectomy and lymphadenectomy without peritoneal insufflation for sigmoid colon cancer patients. Dis Colon Rectum 38: 550–552
171. Alexander RJ, Jaques BC, Mitchell KG (1993) Laparoscopically assisted colectomy and wound recurrence. Lancet 341: 249–250
172. O'Rourke N, et al. (1993) Tumor inoculation during laparoscopy. Lancet 342: 368
173. Walsh DC, Wattchow DA, Wilson TG (1993) Subcutaneous metastases after laparoscopic resection of malignancy. Aust N Z J Surg 63: 563–565
174. Fusco MA, Paluzzi MW (1993) Abdominal wall recurrence after laparoscopic-assisted colectomy for adenocarcinoma of the colon: report of a case. Dis Colon Rectum 36: 858–861
175. Cirocco WC, Schwartzman A, Golub RW (1994) Abdominal wall recurrence after laparoscopic colectomy for colon cancer. Surgery 116: 842–846
176. Nduka CC, et al. (1994) Abdominal wall metastases following laparoscopy. Br J Surg 81: 648–652
177. Champault G, et al. (1994) [Neoplastic colonization of trocart paths: should laparoscopic surgery be stopped for digestive cancers? Presse Med 23: 1313
178. Ramos JM, et al. (1994) Laparoscopy and colon cancer: is the port site at risk? A preliminary report. Arch Surg 129: 897–899 discussion 900
179. Cohen SM, Wexner SD (1993) Laparoscopic colorectal resection for cancer: the Cleveland Clinic Florida experience. Surg Oncol 2(Suppl 1): 35–42
180. Jacquet P, et al. (1995) Cancer recurrence following laparoscopic colectomy: report of two patients treated with neated intraperitoneal chemotherapy. Dis Colon Rectum 38: 1110–1114