

Laparoscopic Resection of Colonic Carcinoma EAES consensus conference Lisbon, June 2, 2002

CONSENSUS PROCEEDINGS

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1 INTRODUCTION

Laparoscopic surgery for colonic cancer remains controversial. Many surgeons have abandoned the laparoscopic approach for resection of colon cancer because of early reports of port site metastases despite evidence from experimental tumour biology studies that have indicated clear oncological benefit of laparoscopic surgery.

Clinical trials randomizing patients with colonic cancer to either laparoscopic or open resection were initiated in the mid 90's to assess the oncological safety of laparoscopic surgery. As a minimum follow-up period of 3 years is required to establish cancer-free survival rates, none of these ongoing randomized trials has, as yet accumulated sufficient data that enable reliable and definite adjudication.

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

The objectives of the consensus conference are:

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

2 METHODS

The consensus recommendations and statements are based on (i) a systematic review of the literature, (ii) a consensus development conference (CDC) and (iii) a meta-analysis of patient data from two large randomized trials.

A panel of experts in both open and laparoscopic surgery was 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 colonic cancer, participate in the CDC and review/ modify 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 sent to them. The questionnaire covered key aspects of laparoscopic resections of colonic cancer. Personal experience of the experts, their opinion or references included from the literature search were the basis to complete the questionnaire. In parallel, the questions were addressed by 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 as the previous query was too restricted and hence inappropriate for the Cochrane database. Relevant articles were first selected by title, and then their relevance to the objectives of the CC 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 (RCTs). However, other reports, e.g., using concurrent cohort, external or historical controls, population-based outcomes studies, case series and case reports were included but all the articles were categorized in terms of the quality of data and evidence they provided by two reviewers (Table 1).

Grade of recommendation	Level of evidence	Possible study designs for the evaluation of therapeutic interventions
A	1a	Systematic review (with homogeneity) of RCTs
	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

Table 1: A method for grading recommendations according to scientific evidence*

(* Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. Evidence-based medicine: How to practice and teach EBM. (2nd Ed.) London/UK: Churchill Livingstone, 2000.)

The systematic review of the literature provided evidence on: extent of the resection, morbidity, hospital stay, recovery, costs and mortality of laparoscopic colonic cancer surgery. Regrettably, the level of evidence of articles on surgical technique is low by 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, surgical experience etc., cannot be measured objectively. The pooled data of the 2 randomized clinical trials (Barcelona trial and COLOR trial) were analyzed separately to provide an initial assessment of the oncological safety of laparoscopic resection of colonic cancer before the CDC in Lisbon.

Analysis of the completed questionnaires, the culled information from the systematic review as outlined above and the analysis of pooled data 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 June 2, 2002. All statements / recommendations and clinical implications with grades of recommendation were discussed during a 6-hour 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 (1½ hour session). During a post-consensus meeting on the same day, all suggestions from the audience were discussed by the panelists, and the consensus document modified where appropriate. The final proceedings were approved by all the panelists before publication.

3 PREOPERATIVE EVALUATION AND SELECTION OF PATIENTS

3.1 Preoperative imaging

In current practice, the same preoperative work-up is done prior to both laparoscopic and conventional colectomies. Colonoscopic biopsy is done in most patients to confirm presence of cancer. Colonoscopy does not accurately localize the lesion [1]. Metastatic spread is commonly investigated by ultrasonography of the liver and plain radiography of the chest. Abdominal CT imaging to assess the size of the tumor and possible invasion of adjacent tissues is performed selectively in some European centres and more extensively in the USA. Laparoscopy has the potential for assessing tumor invasion of adjacent organs but there are no published reports with respect to the value of laparoscopic staging in the workup and selection of patients for open or laparoscopic resection of colonic cancer as distinct from established use in gastric, pancreatic and oesophageal tumours. Another unresolved issue relates to timing of the laparoscopic staging, e.g., immediately prior to the resection or in a separate. This has implications on scheduling of cases.

Conventional computed tomography of the colon can provide information about the localization of the tumor. However, more advanced radiologic techniques such as virtual colonoscopy can assess the site of the tumor more precisely.

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 tumour size improves selection and reduces the need for conversion.

Cancerous invasion of organs adjacent to the colon can be detected by computed tomography. However, the accuracy of preoperative staging of colonic cancer by CT varies from 40 to 77 % [2] because of the limited soft tissue contrast of CT which impairs assessment of mural invasion by the tumour. The importance of tumour 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 chapter: Conversion rate).

Recommendation 1: Preoperative imaging

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

3.2 Contra-indications

3.2.1 Age

The experts agreed that age is not a contraindication. This view is supported by a sub analysis of a case series by Delgado et al.[3] who reported significantly lower morbidity after laparoscopic resection compared to open colectomy in patients over 70 years. In the study by Schwandner et al.[4], 298 patients undergoing laparoscopic or laparoscopic-assisted colorectal procedures, there were no statistically significant differences between the younger, middle-aged, and older patients in terms of conversion rate (3.1 vs. 9.4 vs. 7.4 percent, respectively), major complications (4.6 vs. 10.1 vs. 9.5 percent, respectively) and minor complications (12.3 vs. 15.2 vs. 12.6 percent, respectively). However, duration of surgery, stay in the intensive care unit, and postoperative hospitalization were significantly longer in patients older than 70 years ($P < 0.05$).

Statement 2: Contra-indications: age

	Level of evidence	Recommendation
Age only is not a contra-indication for laparoscopic resection of colonic cancer.	2b	-

3.2.2 Cardiopulmonary condition

Cardiopulmonary consequences of the pneumoperitoneum have been thoroughly reviewed in the EAES consensus statement of 2001[5]. Relevant parts of this consensus have been enclosed in the current consensus. Decreased cardiopulmonary function is not regarded a contraindication to laparoscopic resection of colonic cancer.

Cardiovascular effects of pneumoperitoneum occur most often during its induction, and this should be considered when initial pressure is raised for 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 pneumoperitoneum causes hypercapnia and respiratory acidosis. During laparoscopy, monitoring of end-tidal CO₂ concentration is mandatory (grade A) and minute volume of ventilation should be increased in order to maintain normocapnia. Increased intra-abdominal pressure and head-down position reduce pulmonary compliance and lead to ventilation-perfusion mismatch (grade A). In patients with normal lung function, these intra-operative respiratory changes are usually not clinically relevant (grade A). In patients with limited pulmonary reserves, capnoperitoneum carries an increased risk of CO₂-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 intra-abdominal 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: Contra-indications: cardiopulmonary status

	Level of evidence	Recommendation
Invasive monitoring of blood pressure and blood gases is mandatory in ASA III-IV patients (No consensus: 91% agreement among experts)		Grade A
Low pressure (lower than 12 mm Hg) pneumoperitoneum is advocated in ASA III –IV patients		Grade B

3.2.3 Obesity

Intra-operative 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 68% higher than normal [6]. 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.

Pandya [7] has shown that the conversion rate is higher in patients with a Body Mass Index (BMI) greater than 29 due to increased technical difficulties. A similar conclusion was reached by Pikarsky who reported a higher conversion rate in patients with a BMI above 30 [8].

Statement 4: Contra-indications: obesity

	Level of evidence	Recommendation
Obesity is not an absolute contra-indication but the rates of complications and conversions are higher at BMI greater than 30 (No consensus: 93% agreement among experts).	2c	-

3.2.4 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[9]. Laparoscopic radical resection of locally advanced colorectal tumors is problematic because adequate laparoscopic atraumatic retraction of bulky tumors is difficult. Furthermore, laparoscopic resection of adjacent involved organs or 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 a T4 colonic cancer as an absolute contra-indication to laparoscopic resection, en bloc laparoscopic resection being possible only in a limited number of patients.

The laparoscopic approach is useful for palliative resections of colonic cancer. The majority of experts does not consider peritoneal carcinomatosis to be a contra-indication for laparoscopic surgery.

Recommendation 5: Contra-indications: tumor characteristics

	Level of evidence	Recommendation
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

3.2.5 Adhesions

Adhesions account for 17 % of all conversions. However, prior abdominal surgery appears to play a less important role in the completion rate of laparoscopic colon surgery as reported by Pandya[7]. In this study, conversion rates did not differ between patients who had previous abdominal surgery 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 intra-abdominal adhesions. Hamel et al. [10] compared the morbidity rate between patients with and without prior abdominal surgery. The complication rates were similar between the two groups despite the presence of more adhesions in the previously operated group.

Statement 6: Contra-indications: adhesions

	Level of evidence	Recommendation
Adhesions are not a contra-indication to laparoscopic colectomy.	4	-

3.2.6 Localization

Half the experts does 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.

4 OPERATIVE TECHNIQUE

4.1 Anesthesia

Nitrous oxide when employed as inhalational anesthetic does not cause intestinal distension assessed by girth of transverse colon and terminal ileum at the beginning and end of surgery [11].

The first study investigating the usefulness of nitrous oxide during laparoscopic surgery was completed by Taylor[12]. In one group, isoflurane with 70% N₂O in oxygen (O₂) was used, in the other; isoflurane in an air/O₂ 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.

The majority of experts employ general anesthesia without epidural analgesia.

4.2 Pneumoperitoneum

Recommendations regarding the creation of a pneumoperitoneum are given in the EAES consensus statement of 2001[5].

4.3 Trocars position

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 3 trocars and 20% 5 trocars. The majority extracts the specimen through an incision made at the site of the umbilical trocar. At the umbilicus a 10-12mm trocar is placed. A 10mm trocar is placed suprapubically and in the epigastric region by 70% of authors. Some experts place a 5mm trocar at the left iliac fossa or at the right subcostal space.

For left hemicolectomy and for sigmoid resection, trocars are positioned almost at the same sites. Thirty percent of experts perform these procedures using the hand-assisted technique. Five trocars are used by over 70% of experts. A 10-12mm trocar is placed at the umbilicus; two 10mm 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.

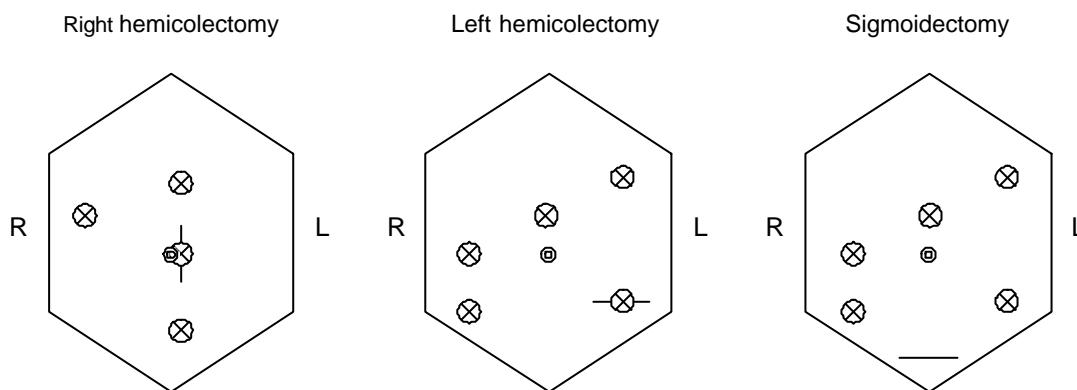


Figure 1: An example for placement of trocars and retraction ports

Statement 7: Placement of trocars

	Level of evidence	Recommendation
Placement of trocars is based on the experience and the preference of the individual surgeon.	5	-

4.4 Camera

There is unanimous agreement about the use of a 3-chip camera, because of its better resolution. The laparoscope can be 30° or 0°, depending on the surgeon's preference. One expert uses a videolaparoscope. The camera is hand held by the majority of experts. Mechanical and robotic devices are available, but are used by less than 10% of experts.

Recommendation 8: Type of camera

	Level of evidence	Recommendation
High quality videoscopic imaging and instrumentation is strongly recommended.	5	Grade D

4.5 Prevention of port site metastasis

4.5.1 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 below 1%. Surgical experience thus appears the main determinant for the occurrence of port site metastases.

4.5.2 Wound protectors

Experimental studies have shown that tumor growth at the site of extraction of a malignant tumor is increased[13]. All experts protect the abdominal wall or place the specimen in a plastic bag prior to extraction to prevent tumour cell implantation/ growth. However, since neoplastic recurrence has been documented at the extraction site after removal of a right colonic cancer which was placed in a plastic bag, the benefit of such devices is questionable [14]. Wound protection is considered safer.

4.5.3 Gasless laparoscopy

In view of the possibility that a positive pressure pneumoperitoneum may be responsible for wound tumour deposits, some have suggested the use of gasless laparoscopy. In this respect, experimental findings on gasless laparoscopy are controversial. Although Bouvy et al.[13] and Watson et al.[14] reported a significant decrease in the occurrence of port site metastasis when gasless laparoscopy was used in an animal model, Gutt et al.[15] and Iwanaka et al.[16] could not confirm these observations. Wittich et al. in an experimental study reported that tumor growth was proportional to the insufflation pressure[17]. Hence low insufflation pressures may reduce the risk of dissemination.

4.5.4 Different types of gas

Carbon dioxide attenuates the local peritoneal immune response, which might enhance the risk of tumour cell implantation and tumour growth in the traumatized tissues. Neuhaus and Jacobi [18] 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.

4.5.5 Wound excision.

As cancer cells implant in wounds during surgery, it might be expected that excision of the wound should reduce the rate of neoplastic wound recurrences. This has not been confirmed in animal studies. Thus, Wu et al.[19] found that wound excision reduced the rate of port site metastases from 89% to 78% but did not eliminate them, and Watson et al reported that wound excision was followed by a significant increase of wound recurrence[20].

4.5.6 Irrigation of peritoneal space and port site

Some authors have suggested that irrigation of the peritoneal cavity with various solutions can reduce the incidence of wound metastases. Animal studies have shown that peritoneal irrigation with povidone-iodine[21, 22], heparin[23], methotrexate[21], and cyclophosphamide [16] all reduced the rate of port site metastasis. Intraperitoneal tumor growth and trocar metastases were suppressed by the use of tauridine in a rat model[24-26]. Half of the experts irrigate the peritoneal space with betadine, distilled water or tauroline. Eshraghi et al.[27] 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.

4.5.7 Trocar fixation

Tseng et al.[28] 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.

4.5.8 Aerosolization

In experimental studies[29, 30], aerosolization is only possible with very large numbers of tumor cells in the abdominal cavity. The clinical significance of aerosolization of tumour cells is not proven. Some experts advocate desufflation of the pneumoperitoneum at the end of the operation before removal of the ports.

4.5.9 No-touch technique

The no touch technique is based on the risk of tumor emboli from manipulation of the tumour during resection of colorectal carcinomas. The value of the no-touch technique in colon surgery remains debatable. An improvement in the 5-year survival was reported by Turnbull et al in a retrospective analysis [31] but subsequently in the only prospective, randomized trial evaluating 236 patients, Wiggers et al.[32] demonstrated 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.

4.5.10 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[9]. Exfoliated tumour cells have been detected in resection margins, rectal stumps, and circular stapling devices[33-35]. Furthermore, the viability and proliferative and metastatic potential of exfoliated malignant colorectal cells have been confirmed [34, 35]. Several washout solutions, including normal saline, have been shown to eliminate exfoliated malignant cells in the doughnut of rectal tissue from circular staplers[36]. Despite these observations there is no conclusive evidence that bowel washouts reduce local recurrence and hence no data support their use in colon cancer. However, with no risk and minimal cost, bowel washout may have some utility in the management of rectal cancer, where the anastomotic and the cancer sites are close to each other.

Statement 9: Preventive measures for port site metastasis

	Level of evidence	Recommendation
Proper surgical technique and practice reduces the likelihood of port site metastasis.	3a	-

4.6 Tumor localization

Pre-operative tumor localization is important in laparoscopic resection of colonic cancer as intraoperative localization by palpation of the colon for tumours, 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 include resection of the wrong bowel segment or incomplete or non-radical resection because of insufficient proximal or distal margin[37-39].

Many colonoscopic techniques are used for marking the site of a tumour. Two of these, metal clip placement[40, 41] and tattooing [42, 43] are most commonly used. Localization is advisable except for tumors located near the ileo-caecal valve which forms a clear landmark during colonoscopy [44]. Special equipment is needed for clip placement. Before surgery, plain abdominal radiography is performed to exclude migration of clips. During surgery, the clips are identified by intra-operative ultrasound or fluoroscopy. Hence this is an expensive and time consuming technique[45] although it is very reliable[41, 46].

Intra-operative colonoscopy is an alternative modality to localize the colonic lesion. However, this technique induces distention of the colon and small bowel, particularly in right sided lesions[47].

The colonoscopic tattooing technique with Indian 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 the 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%[43, 48].

The reported morbidity rate for tattooing is 0.22% [49]. In this review, only one patient was found in whom overt clinical complications developed. Injection into the peritoneal space is reported in 0.5% to 8%[45, 50].

Recommendation 10: Intraoperative localization of tumor

	Level of evidence	Recommendation
Preoperative tattooing of small colonic tumors is advised. The alternatives are intraoperative colonoscopy, or pre-operative colonoscopic clipping followed by peroperative fluoroscopy or ultrasonography. Peroperative ultrasonography can be employed as well at the hands of experts.	5	Grade D

4.7 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 disposable EndoGia and 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[51].

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

Hand assisted laparoscopic surgery (HALS) is an alternative to laparoscopically-assisted colectomy. This procedure allows the surgeon to use his 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 tumours 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 [52]. HALS appears to be at least as effective as the laparoscopically-assisted technique in terms of operative time, conversion rate and post-operative outcome[53]. Only two experts use HALS for laparoscopic colectomy.

4.8 Dissection of mesocolon

Most experts perform mesocolic dissection and secure the mesocolic vessels at the start of the colonic resection. Fifty-four percent of experts use a vascular stapling device, 27% employ an external knotting technique and 18% place clips to secure the main mesocolic vessels. The majority of experts dissect the Toldt fascia from medial to the lateral side.

For right hemicolectomy, the mobilization of the bowel is always performed laparoscopically. Dissection of the mesocolon is also done laparoscopically. Bowel transection can be performed both 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 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

	Level of evidence	Recommendation
Dissection of the mesocolon from medial to lateral is the preferred approach in laparoscopic colonic surgery. During hand-assisted laparoscopic surgery for colonic cancer, the mesocolon can also be resected from lateral to medial.	5	Grade D

4.9 Learning curve

“Learning curve” can be defined in various ways. Simons considered the learning curve completed when the operative time stabilizes and does not vary by more than 20 minutes [54]. Schlachta et al. [55] determined that the learning curve for performing colorectal resections involved 30 operations when operating time, intraoperative complications, and conversion rate decline. Bennett et al.[56] reported that experience plays an important role in reducing complication rates, and has less impact on reducing operating time.

Lezoche et al. reported that the conversion rate dropped from 17 to 2% after 30 laparoscopic colectomies[57]. Many consider the learning curve for laparoscopic colon resection to be longer than that for laparoscopic cholecystectomy.

5 INTRAOPERATIVE RESULTS OF LAPAROSCOPIC RESECTION OF COLONIC CANCER

5.1 Conversion rate

Study	N	Conversion rate	Cause
1			
Weeks[58]	58/228	25%	11 advanced disease, 3 positive margins, 10 inability to visualize structures, 4 inability to mobilize colon, 12 adhesions, 4 intraoperative complications, 2 associated complicating disease, 12 other
2			
Schwenk[59]	0/30	0%	After diagnostic laparoscopy
Milsom[60]	4/59	7%	2 bowel distension, 1 tumor too low, 1 adhesions
Delgado[3]	18/129	14%	15 invasion adjacent organs, 1 adherence, 2 NS
Curet[61]	7/25	28%	3 tumor fixation to adjacent organs, 3 extensive adhesions, 1 abscess around ureter
Stage[62]	3/18	17%	3 extensive tumor growth
Lacy[63]	4/25	16%	4 invasion small bowel
3			
Lezoche[64]	6/140	RHC 0% LHC 7% Total 4%	2 hemorrhage, 2 anastomotic defects, 1 obesity, 1 inadequate splenic flexure mobilization
Lezoche[65]	5/104	4.8%	2 anastomotic defects, 1 obesity, 1 inadequate splenic flexure mobilization, 1 hemorrhage
Bouvet[66]	38/91	42%	12 adhesions, 8 poor exposure, 5 extensive tumor growth, 3 excessive procedure time, 2 bleeding, 2 inability to identify the ureter, 1 inadequate distal margin, 1 equipment failure, 4 combination of factors
Hong[67]	12/98	12%	5 adherence, 5 size of tumor, 2 adhesions
Psaila[68]	3/25	12%	NS
Khalili[69]	6/80	8%	3 extensive tumor, 2 adhesions, 1 intraoperative bleed
Pandya[7]	47/200	23.5%	6 hypercarbia, 2 unclear anatomy, 2 stapler misfiring, 5 too ambitious, 6 bleeding, 1 cystotomy, 2 enterotomy, 5 adhesions, 3 obesity, 10 size/invasion tumor, 5 phlegmon
Bokey[70]	6/34	18%	1 injury caecum, 1 adherence, 1 adhesions, 1 hypercapnia, 2 lack of progress
Franklin[71]	8/192	4.2%	7 large invasive tumor, 1 bleed
Santoro[72]	0/50	0%	-
Leung[73]	8/50	4%	2 adhesions, 2 bleeding, 3 large/ invasive tumors, 1 low tumor
Van Ye[74]	1/15	6.7%	1 adhesions
Leung[75]			
4			
Schiedeck[76]	25/399	6.3%	NS
Bokey[77]	9/66	14%	2 lack of progress, 2 adherence, 1 adhesions, 1 caecal injury, 1 hypercapnia, 1 ureter not identified, 1 bleed
Fleshman[78]	58/372	15.6%	NS
Franklin[79]	3/50	6%	3 bulky/invasive tumor
Poulin[80]	12/131	9%	6 fixed tumor, 3 adhesions, 1 oncologic resection impossible, 1 hemorrhage, 1 perforation small bowel
Leung[81]	54/201	26.9%	22 conversions after diagnostic laparoscopy (not clarified)
Total	395/2769	14.3%	Invasive or bulky tumor: 36% Adhesions: 18% Technical problem: 22% (12 lack of progress, 18 poor exposure, 8 hypercarbia, 6 anastomotic problem, 2 bowel distension, 6 inadequate mobilization, 1 equipment failure) Bleed: 7% Safe oncol resection impossible: 2% Visceral injury: 3% Obesity: 2% Others: 10%

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

NS = not specified

Reported conversion rates in laparoscopic surgery depend on the definition of conversion, selection of patients and 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[60, 82]. If the laparoscopic findings indicated that resection

was not possible laparoscopically, open surgical resection was performed. These operations were not considered as converted. In two case series high conversion rates were reported of 41% and 48% [83, 84]. 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 [38, 82, 85-88].

In a study by Lezoche, conversion rates were calculated for the first 30 patients operated laparoscopically and for the consecutive 26 patients. The conversion rate in the early experience group was 16.8% and in the subsequent group 1.8%, indicating the importance of experience in reducing the conversion rate [64]. This is confirmed by several other reports analyzing early with later experiences [7, 38, 86, 89]. All found a clear decrease in the number of conversions as more operations were performed.

Laparoscopic colectomies are converted for a wide variety of reasons. Locally advanced bulky or invasive tumors, adhesions and technical problems account for the majority of the 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 invasion of surrounding structures.

Statement 12: Conversions

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

5.2 Duration of surgery

Study	Operating time		Significance
	Laparoscopic	Open	
2			
Hewitt[90]	165	107.5	P=0.02
Milsom[60]	200±40	125±51	P<0.0001
Delgado[3]	<70 yrs: 144±40 >70 yrs: 150±60	122±45 119±51	P=0.005 P=0.001
Curet[61]	210(128-275)	138(95-240)	P<0.05
Stage[62]	150 (60-275)	95 (40-195)	P=0.05
Lacy[63]	148.8±45.5	110.6±49.3	P=0.006
Schwenk[91]	219±64	146±41	P<0.01
3			
Lezoche[64]	RHC 190 First 30: 226 Last 20: 153	140	P=0.03
	LHC 240 First 30: 260 Last 20: 210	190	P=0.04
Bouvet[66]	240 (150-516)	150 (60-376)	P<0.01
Fukushima[92]	231	169	NS
Hong[67]	140±49.5	129±53.5	NS
Psaila[68]	179±41	123±41	P<0.05
Khalili[69]	161±7	163±8	NS
Lezoche[57]	Mean 251 (90-480) RHC 203 (90-330) LHC 282 (150-480)	175 (90-340) 140 (90-280) 190 (130-340)	P<0.001 P<0.001 P<0.001
Marubashi[93]	RHC 211.9 (134-330)	148.7 (104-173)	P<0.05
Leung[73]	196±44.4	150±61.1	P<0.001

Table 3: duration of surgery

n.a. = not available, NS = not significant, values are given as mean or percentage if followed by [%] or median if followed by [+], between brackets range is given, after [±] SD is given. RHC= right hemicolectomy, LHC= left hemicolectomy, yrs = years

In general, laparoscopic resection of colonic cancer takes longer to perform than open resection. Although operating time decreases with increasing experience[57, 64, 83, 86, 94], it is difficult to compare operating times between open and laparoscopic resections for colonic cancer because most studies include a wide variety of procedures and do not specify per type of resection performed. Studies which included rectal procedures reported longer operating times[60, 61, 66].

Reported operating times vary between 140-251 minutes for laparoscopic colorectal resections and 120-175 minutes for open surgery [Table 3]. In some studies benign lesions were also included [60] and rectal procedures were excluded in only one RCT [63]. In 2 RCTs[60, 61] and in 5 non-randomized comparative studies the "intention to treat" principle was violated[57, 66, 69, 73, 93], resulting in selection bias, possibly favoring the laparoscopic group.

Statement 13: Duration of surgery

	Level of evidence	Recommendation
Laparoscopic colectomy requires more operating time than open colectomy.	2a	-

5.3 Extent of resection

Study	No of lymph nodes			Resection margins (cm)		
	Lap	Open		Lap	Open	
2						
Milsom[60]	19 +	25	--	Clear in all	Clear in all	
Delgado[3]	<70 yrs 9.6 >70 yrs 12.2	10.5 10.5	NS NS			
Curet[61]	11	10	NS	Length 26	25	--
Stage[62]	7	8	--	Margins 4	4	
Lacy[63]	13	12.5	NS			
3						
Lezoche[64]	RHC 14.2 LHC 9.1	13.8 8.6	NS NS	Length 28.3 Length 22.9 LHC TFM 5.2	29.1 24.1 5.3	NS NS NS
Bouvet[66]	8	10	NS	Prox 10 Dist 6	10 9	NS P=0.03
Hong[67]	7	7	NS	Dist 7,9	7,2	NS
Koehler[95]	14	11	--	Length 24.1 Prox 13.2 Dist 7.9	22.6 10.1 8.6	-- -- --
Psaila[68]	7,0	7,7	NS			
Khalili[69]	12	16	--			
Lezoche[57]	10,7	11	NS	Length 26.8 LHC TFM 5.2	29.4 5.3	NS NS
Marubashi[93]	1,7 (Level of dissection)	2,25	P<0.01			
Bokey[70]	17	16	NS	Prox 10,1 Dist 10,0	11,9 13,4	NS P=0.03
Franklin[71]	Lap not different from open			Length of specimen + number of lymph nodes not different		
Santorof[72]						
Leung[73]	9 +	8		Dist 3 +	3,5 +	

Table 4: Number of lymph nodes harvested and extent of resection

n.a. = not given, NS = not significant, Length = length of resected specimen, Prox = proximal margin, Dist = distal margin, LHC = Left hemicolectomy, RHC = right hemicolectomy, TFM = Tumor Free Margin, values are given as mean or percentage if followed by [%] or median if followed by [+]

For a laparoscopic oncological resection to be as safe as an open resection, the extent of colon resection should not differ from that of open colectomy. All RCTs report similar numbers of lymph nodes harvested in laparoscopic versus open surgical specimens. Also the length of the retrieved bowel segments and tumor free margins appear comparable.

In non-randomized comparative studies, no differences between open and laparoscopic groups were found in the number of lymph nodes, the length of the retrieved specimen, tumor free proximal and distal margins and total length of specimen. In two studies, a shorter distal resection margin was recorded[66, 70]. However, in these studies the mean distal tumor free resection margins were still 6 and 10 cm respectively.

There are reports of laparoscopic colon resections not containing the primary tumor or missing a synchronous second colonic carcinoma. This stresses the importance of tumor localization by either tattooing the tumor with ink or intraoperative colonoscopy.

Statement 14: Extent of resection

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

6 CLINICAL OUTCOME

6.1 Short-term

6.1.1 Morbidity

Study	Morbidity		Significance
2	Lap	Open	
Milsom[60]	15%	15%	NS
Delgado[3]	Mean 10.9%	25.6%	P=0.001
	<70 yrs 11.4%	20.3%	NS
	>70 yrs 10.2 %	31.3%	P=0.0038
Curet[61]	1.5%	5.28%	NS
Stage[62]	11%	0%	--
Lacy[63]	8%	30.8% s	P=0.04
Schwenk[59]	7%	27%	P=0.08
3			
Lezoche[64]	RHC 1.9%	2.3%	NS
	LHC 7.5%	6.3%	NS
Bouvet[66]	24%	25%	NS
Hong[67]	Major 15.3%	14.6%	NS
	Minor 11.2%	21.5%	P=0.029
Koehler[95]	No overall number		no statistics
Khalilj[69]	19%	22%	NS
Lezoche[57]	Total 13%	14.3%	NS
	Minor 3.6%	7.5%	NS
	Major 9.4%	6.8%	NS
Marubashi[93]	27.5%	25%	--
Bokey[70]	No overall number		Diff per complication: NS
Franklin[71]	Early 17%	23.8%	no statistics
	Late 5.2%	8.9%	
Santorio[72]	Early 28%	28%	--
	Late 12%	0%	
Leung[73]	26%	30%	NS

Table 5: Morbidity

NS = not significant

The reported morbidity and mortality rates for open conventional colorectal surgery range from 8 to 15% and 1 to 2 % respectively[96]. The serious complications include anastomotic leakage, bowel obstruction and infection.

The data from the RCTs indicated a significantly lower overall complication rate after laparoscopic surgery[3, 63]. In a subset analysis, comparing laparoscopic to open resection in patients over 70 years of age, the reduction of postoperative morbidity after laparoscopic resection is more pronounced than in patients under 70 years of age[3].

Morbidity of laparoscopic resection of colonic cancer has not been reported in sufficient detail by most authors[97]. Specific complications of laparoscopic surgery involve vessel injuries, trocar site hernias[74, 98], and transection of the ureter[84]. Visceral injuries are mainly caused by blind introduction of the Veress needle or first trocar or during dissection of adhesions [83, 84, 97]. Winslow et al. reported incisional hernia at the extraction site in 19 % after laparoscopic surgery while incisional hernias occurred in almost 18 % after open colectomy[99].

Experience is important in preventing complications. In three studies, the morbidity declined with increasing experience [38, 56, 89]. A recent systematic review [96] analyzed the morbidity (Table 6) reported in 11 studies [62, 63, 73, 75, 77, 81, 90, 100-103].

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

Table 6: Complication rates in an analysis of 11 studies

Infectious complications of laparoscopic colectomy have not been assessed by large-scale prospective randomized studies. A reduced incidence of wound infection has been documented in a RCT for laparoscopic compared to open appendectomy[104]. In a systematic review on laparoscopic versus open appendectomy, wound complications were more frequent after open appendectomy [pooled odds ratio for 10 studies: 2.6 (95% CI 1.3-5.2)][105]. Wound infection at the extraction site was encountered in 14 % of patients after laparoscopic colectomy versus 11 % of patients after open colectomy [99].

Statement 15: Morbidity

	Level of evidence	Recommendation
Morbidity after laparoscopic colectomy does not differ from that after open colectomy.	2b	-

6.1.2 Mortality

Mortality rates, defined as mortality within 30 days after surgery, are similar for both open and laparoscopic colectomy. However, no randomized controlled trials have been conducted so far with sufficient numbers to distinguish small differences. In 2 RCTs, a 0% mortality rate has been reported for both open and laparoscopic procedures [90, 106]. In the RCT by Scwenk et al.[59] one death occurred in the conventional group and none in the laparoscopic group. In one RCT, 3 deaths occurred, but this study failed to report to which group patients were assigned to and the cause of death[62].

In non randomized reports, mortality was only reported in five studies[67, 70, 72, 75, 95]. 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

	Level of evidence	Recommendation
Mortality of laparoscopic colectomy appears similar to that of open colectomy.	2b	-

6.2 Recovery

6.2.1 Length of hospital stay

Study	Length of hospital stay (days)		
	Lap	Open	
1			
Weeks[58]	5.6 ±0.26	6.4±0.23	p<0.001
2			
Hewitt[90]	6	7	--
Milsom[60]	6.0 (3-37)	7.0 (5-24)	NS
Delgado[3]	<70 yrs 5	7	P=0.0001
	>70 yrs 6	7	P=0.0009
Curet[61]	5.2	7.3	P<0.05
Stage[62]	5	8	P=0.01
Lacy[63]	5.2	8.1	P=0.0012
3			
Lezoche[64]	RHC 9.2	13.2	P=0.001
	LHC 10.0	13.2	P=0.001
Bouvet[66]	6	7	P=0.01
Hong[67]	6.9	10.9	P=0.003
Koehler[95]	8.1	15.3	--
Psaila[68]	10.7	17.8	P=0.001
Khalili[69]	7.7	8.2	NS
Lezoche[57]	10.5	13.3	P=0.027
Marubashi[93]	18.7	35.8	P<0.0001
Franklin[71]	<50 yrs 5.2	9.35	--
	>50 yrs 7.84	12.85	
Leung[73]	6	8	P<0.001

Table 7: Length of hospital stay

NS = not significant, values are given as mean or median if followed by [+], between brackets range is given, after [±] SD is given

Many factors determine length of hospital stay after surgery. This differs with country and hospital. Clinical condition of the patient is only one factor determining length of hospital stay after surgery. Type of insurance, social and economic status and perception of both surgeon and patient of postoperative recovery are important factors. The COST trial by Weeks et al.[58] is currently the only multi-center RCT with the highest power and published data. In this trial, a highly significant shorter hospital stay was found after laparoscopic colectomy.

Six other RCTs reported on length of hospital stay[3, 60-63, 90]. In one RCT with a sample size of 16, no statistical analysis was performed[90]. Median and range of length of hospital stay did not differ in this study (6 (5-7) vs. 7 (4-9) days). In four other RCTs, a significant earlier hospital discharge has been reported in the laparoscopic group[3, 61-63]. In one RCT, the difference was not significant[60]

In the non-randomized comparative studies, hospital stay after laparoscopic surgery varies from 5.7 to 18.7 days and between 8 and 35.8 days after open surgery[57, 64, 66-69, 71, 73, 93, 95]. In all these studies, hospital stay was shorter in the laparoscopic group, although in three studies differences were not significant[69, 95, 107]. Differences vary from 1 to 7 days.

In a recent article by Wilmore et al.[108] 'fast track' surgery for open procedures has been reviewed. Fast track surgery is a multimodal approach, which combines various techniques used in the perioperative care of patients to accomplish a faster recovery and dismissal after surgery. Methods used 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 two days after conventional open colectomy. So far, this approach has not been studied for patients who underwent a laparoscopic resection of colonic cancer.

Statement 17: Length of hospital stay

	Level of evidence	Recommendation
Hospital stay after laparoscopic resection of colonic cancer is shorter than after open colectomy.	1a	-

6.2.2 Postoperative pain

Postoperative pain is an endpoint, which impacts on the perceived health status, quality of life, hospital stay and resumption of normal activities. In general, postoperative pain is perceived to be less severe following endoscopic surgery than following open surgery. In one RCT, statistically significantly less pain at rest after laparoscopic resection of colonic cancer was observed for up to 30 days postoperatively, when compared to open colectomy[62]. Also pain during mobilisation was reported to be less severe. The number of patients included in this trial, however, was limited and the methodology used was flawed as the 'the intention to treat principle' was violated. Similar results were obtained by another RCT[95]. This showed differences in pain at rest and during mobilization for up to 12 days but these were not significant. In a recent RCT postoperative pain was analyzed using the Symptoms Distress Scale which includes self reported symptoms like pain along with the duration of use of analgesics[58]. In this study, only a shorter duration of use of analgesics was observed in the laparoscopic arm.

Statement 18: Pain

	Level of evidence	Recommendation
Pain is less severe after laparoscopic colectomy.	2a	-

6.2.3 Postoperative analgesia

Study	Analgesics		Lap	Open	Significance
1					
Weeks	Oral (days)		2.2 ±0.15	1.9± 0.15	P=0.03
	Parenteral (days)		4.0± 0.16	3.2 ±0.17	P<0.001
2					
Milsom[60]	Morfine	Day 1	0.78±0.32	0.92±0.34	P=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[109]	PCA(morfine)	Cumulative dose untill day 4	0.78(0.24-2.38)	1.37(0.71-2.46)	P<0.01
Hewitt[90]	Morfine	Cumulative dose untill day 2	27(0-60)	62(28-88)	P=0.04
3					
Hong[67]	Days till stop iv or im		2.7±1.5	3.2±2.0	P=0.021
Lezoche[57]	Analgesics in percentage of patients	Day 1	75%	98%	p<0.001
		Day 2	49%	91%	p<0.001
		Day 3	10%	71%	p<0.001
		Day 4	0.7%	49%	p<0.001
		Day 5		21%	
Marubashi[93]	Days till stop epidural		2.98	4.04	P<0.05
	Nr of pills		1.49	2.68	NS
Bokey[70]	Days till stop (parental analg.)		4.4	4.9	NS
Leung[73]	Nr of injections (median)		3 (0-16)	6 (0-32)	P<0.001

Table 8: Postoperative analgesia

NS = not significant, values are given as mean or median if followed by [+], between brackets range is given, after [±] SD is given

Analgesics need after surgery can be measured in several ways. Some authors assessed the number of pills or injections per day[57, 60, 73] while others recorded the number of days the patient needed analgesics[67, 70, 93]. In the COST trial, patients in the laparoscopic arm required parenteral and oral analgesics for a shorter period of time[58]. In another RCT, significantly less morphine was used in the laparoscopic groups only on the first postoperative day[60]. In all other studies, the laparoscopic group used less analgesics, although the difference was not always significant.

Statement 19: postoperative use of analgesics

	Level of evidence	Recommendation
Less analgesia is needed after laparoscopic colectomy compared to open colectomy.	1b	-

6.2.4 Gastro-intestinal function

Study	Flatus/defecation (days)			Bowel movement (days)		
	Lap	Open	P	Lap	Open	P
2 Milsom[60] Delgado[3]	3 (0.8-8)	4 (0.8-14)	P=0.006	4.8 (1.5-8) < 70 yrs 35±36 > 70 yrs 37±19	4.8 (1.5-14.5) 53±26 57±33	NS P=0.0007 P=0.0005
Lacy[63] Schwenk[91]	35.5±15.7 hrs 50±19	71.1±33.6 hrs 79±21	P=0.0001 P<0.01	70±32	91±22	P<0.01
3 Lezoche[64]	<i>Flatus</i> RHC 2.9 LHC 2.7 <i>Stools</i> 3.5 3.8	3.0 3.5 4.0 5.2	NS P<0.0001 P<0.0001 P<0.0001			
Hong[67] Koehler[95]	3±1.7 <i>Defecation</i> 3.4 (2-5)	4,1±1.8 5.8 (3-7)	P<0.0001 --	3.5±2	4,9±2.1	P<0.0001
Khalili[69] Lezoche[57] Marubashi[93] Bokey[70]	3.0 2.1 4.5	3.7 3.75 4.4	NS P<0.0001 NS	3.4 4.9	4.5 5.5	P=0.036 NS

Table 9: Gastro-intestinal function

NS = not significant, values are given as mean or median if followed by [+], between brackets range is given, after [±] SD is given

Study	Parameter	Oral intake		
		Lap	Open	Sign
2 Milsom[60] Delgado[3]	Oral intake	<70 yrs 50±45 >70 yrs 59±33	59±33 81±48	P=0.0001 P=0.002
Curet	Clear liquids Regular diet	2.7 4,1	4,4 5,8	P<0.05 P<0.05
Lacy[63] Schwenk[91]	Oral intake Regular diet	50,9±20 3.3±0.7	98,8±48.6 s 5.0±1.5	P=0.0001 P<0.01
3 Hong[67]	Fluids Solid food	2,1±1.8 5,2±3.1	4,0±2.0 7,1±2.8	P<0.0001 P<0.0001
Koehler[95] Khalili[69]	Regular diet Oral intake	3,2 (2-6) 3,9±0.1	6,2 (4-10) 4,9±0.1	-- P=0.001
Lezoche[57] Marubashi[93] Bokey[70]	Oral intake Fluids Full diet	5,13 4,3 6,9	10,04 4,2 7,6	P<0.0001 NS NS
Leung[73] Van Ye[74]	Normal diet Normal diet	4 (2-20) 4.8	4 (3-17) 7.2	NS P=0.001

Table 10: start of postoperative oral intake

NS = not significant, values are given as mean or median if followed by [+], between brackets range is given, after [±] SD is given

Resumption of intestinal function is measured by several parameters: time to first bowel movement, first passage of flatus or defecation and time to resume intake of liquid or solid foods. In the RCTs, data on passage of first flatus and defecation are consistent with a faster recovery in the laparoscopic

group. Only in two studies, differences were not significant[57, 77]. In all the RCTs, first bowel movement and resumption of diet were faster after laparoscopic colorectal surgery.

Statement 20: Gastro-intestinal function and start of postoperative oral intake

	Level of evidence	Recommendation
Gastro-intestinal function recovers earlier after laparoscopic colectomy.	2b	-

6.2.5 Pulmonary function

Study	Parameters	Lap	Open	Sign
1 Schwenk[59]	FVC	2.59±1.11	1.73±0.60	P<0.01
	FEV1	1.80±0.80	1.19±0.51	P<0.01
	PEF	3.60±2.22	2.51±1.37	P<0.05
	FEF 25-75%	2.67±1.76	1.87±1.12	P<0.05
	SaO2 %	93.8±1.9	92.1±3.3	P<0.05
2 Milsom[60]	FEV1	3.0	6.0	P=0.01
	FVC			
Stage[62]	FEV1	NA		NS
	FVC	NA		
	PEF	NA		

Table 11: Postoperative pulmonary function

NS = not significant, values are given as mean or median if followed by [+], between brackets range is given, after [±] SD is given

Laparoscopic surgery causes less impairment of pulmonary function allowing faster recovery. Postoperative pulmonary function after laparoscopic cholecystectomy, compared to open surgery, is improved[110]. Postoperative pulmonary function after colorectal resections has been investigated in a RCT by Schwenk et al. Parameters shown in Table 11 were measured preoperatively and at different time points postoperatively. The forced vital capacity and the forced expiratory volume were more profoundly impaired in patients having conventional resections than in the laparoscopic group. Similar results were found for the peak expiratory flow and the midexpiratory 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 while none in the laparoscopic group. The difference was not significant, but sample size of the study was only 30 patients.

Postoperative pulmonary function was investigated in two other RCTs (Milsom et al. and Stage et al). Milsom et al.[111] found a significantly earlier postoperative recovery of pulmonary function after laparoscopic surgery. The RCT conducted by Stage et al.[62] showed no significant differences between the two groups.

Statement 21: Postoperative pulmonary function

	Level of evidence	Recommendation
Postoperative pulmonary function is less impaired after laparoscopic compared to open resection of colonic cancer.	1b	-

6.2.6 Return to work / daily activity

These parameters of early recovery are strongly influenced by societal and economic organization of healthcare within a community. This may explain the wide variability between studies. Only in randomized trials one can assume that these factors are evenly distributed in both groups. None of the available randomized trials addressed this topic.

6.3 Long-term outcome of laparoscopic colectomy

6.3.1 Overall survival

Study	Follow-up	Lap	Open
2			
Lacy[106]	21.4±11.5 months	84% (n=31)	90% (n=40)
Delgado[112]	42 months	AR 83%, SR 87% (n=31)	
3			
Leung[75]	21.4 months+	90.9 months(n=28)	55.6 months (n=56)
Leung[73]	32.8 months +	67.2% (n=50)	64.1% (n=50)
Khalili	19.6 months	87.5% (n=80)	85% (n=90)
Santoro	5 years	72.3% (n=50)	68.8% (n=50)
Hong	Lap 30.6 / Open 21.6	(Lap 98 vs Open 219) No significant difference	
4			
Cook[113]	Untill patient death	20% (n=5)	
Hoffman[114]	2 years	Node -: 92% (n=39) Node +: 80%	
Molenaar[115]	3 years	All: 59%, By Dukes staging (n=35): A=86%, B=66%, C=68%, D=0%	
Quattlebaum[116]	8 months	90% (n=10)	

Table 12: overall survival rates

NS = not significant, AR= anterior resection, SR=sigmoid resection

Reliable data on overall survival after laparoscopic colon resections will not be available until the results of large randomized controlled trials are complete. In smaller randomized controlled trials, no differences have been observed between open and laparoscopic surgery. In one RCT involving 91 patients, no significant difference was found in the overall survival[106]. The minimum follow-up period was 12 months with a mean of 21.4 ± 11.5. However, because of small numbers, the power of this study to detect clinically important differences is low[96].

No significant differences were found between open and laparoscopically operated patients In a non-randomized matched control study with 5-year follow-up [75]. 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[73]. In a further 3 comparative studies, no differences of overall survival were found between laparoscopic or open resections of colonic cancer.

6.3.2 Disease-free survival

Study	Follow-up	Lap	Open
3			
Leung[75]	5 years	95.2%	74.7%
Leung[73]	4 years	80.5%	72.9%
Lezoche[65]	48.9 months	86.5%	86.7%
Lezoche[64]	42.2	RHC 78.3	75.8
	42.3	LHC 94.1	86.8
Bouvet[66]	26 months	93%	88%
Santoro[72]	NA	73.2%	70.1%
Hong[67]	Lap 30.6 Open 21.6	NA, diff not sign	
4			
Delgado[112]	42 months	AR: 78% SR: 70%	
Hoffman[114]	2 years	Node - : 96% Node + : 79%	

Table 13 Disease-free survival

NS = not significant, NA = not available

Data on disease-free survival rates are few. None of the RCTs has, as yet, reported disease-free survival. The data from six non randomized studies showed similar disease-free survival [65-67, 72, 73, 75].

6.3.3 Pooled analysis of data

Our goal is to perform a meta-analysis of individual survival data of the four major randomized clinical trials of all patients with 3-year follow-up. At the present time, data of all patients randomized before January 1 1999, and who therefore have sufficient follow-up, of the COLOR and Barcelona trial have been pooled for a preliminary analysis. After exclusion of patients with Duke's D carcinoma, this combined database contains 415 patients (Duke's A: 37, B:236, C:142).

This database was analyzed regarding 3-years disease free survival for safety by the Color statistician WCJ Hop, PhD. As the COLOR and the CLASSICC trials are still recruiting patients, it is not allowed to provide detailed outcome data at the present time. However, his conclusion was that there was no evidence as yet that the laparoscopic approach might lead to a worse survival prognosis. This conclusion was based on the outcomes of a multivariate analysis (Cox-regression) allowing for treatment group, the two trials and Duke's stage. The treatment effect was further found not to differ greatly between both trials (no heterogeneity of treatment effects). More definite conclusion, however, can only be reached if the meta-analysis includes about 1000 patients. Only with such a large number, differences of 8 percent or more in 3-years disease free survival can be excluded with sufficient power.

Statement 22: Overall and cancer related disease free survival

	Level of evidence	Recommendation
No differences of survival between open and laparoscopic resection of colonic cancer have been reported so far. However, data are insufficient to detect clinically important differences of survival between open and laparoscopic colectomy, if such differences existed.	3b	-

6.4 Port-site metastases after laparoscopic colectomy

Study	Design	Patients	Follow-up	PSM
Millsom[60]	RCT	42	Median 18 months	0
Lacy[106]	RCT	31	21.4 months	0
Ballantyne[117]	Registry	498	NS	3
Fleshman[118]	Registry	372	NS	4 (1.3%)
Rosato[119]	Registry	1071	NS	10 (0.93%)
Vukasin[120]	Registry	480	>12 months	5 (1.1%)
Schiedeck[76]	Registry	399	Mean 30 months	1 (0.25%)
Leung[81]	Prospective	217	Mean 19.8 months	1 (0.65%)
Poulin[80]	Prospective	172	Mean 24 months	0
Franklin[71]	Prospective	191	>30 months	0
Bouvet[66]	Prospective	91	26 months	0
Lezoche[65]	Prospective	158	Mean 48.9 months	2
Bokey[77]	Retrospective	66	Median 26 months	1 (0.6%)
Fielding[94]	Retrospective	149	NS	2 (1.5%)
Gellman[121]	Retrospective	58	NS	1 (1.7%)
Hoffman[114]	Retrospective	39	At least 24 months	0
Huscher[85]	Retrospective	146	Mean 15 months	0
Leung[73]	Retrospective	50	>32 months	1 (
Khaliil[69]	Retrospective	80	Mean 21 months	0
Kwok[122]	Retrospective	83	NS	2 (2.5%)
Leung[81]	Retrospective	179	Mean 19.8 months	1 (0.65%)
Lord[98]	Retrospective	71	Mean 16.7 months	0
Lumley[87]	Retrospective	103	NS	1 (1.0%)
Khaliil[69]	Retrospective	80	Mean 19.6 months	0
Guillou[123]	Retrospective	59	NS	1 (1.7%)
Larach[38]	Retrospective	108	Mean 12.6 months	0
Croce[124]	Retrospective	134	NS	1 (0.9%)
Kawamura[125]	Retrospective	67 (gasless)	NS	0
		5194		37 (0.71%)

Table 14 Port site metastasis after resection of colorectal carcinoma

NS = not stated, PSM = port site metastases

Study	Year	Dukes' stage	Months to recurrence
Alexander [126]	1993	C	3
O'Rourke [127]	1993	B	10
Walsh[128]	1993	C	6
Fusco [129]	1993	C	10
Cirocco[130]	1994	C	9
Nduka[131]	1994	C	3
Prasad[131]	1994	B	6
Berends[132]	1994	A	26
		B	NS
		C	NS
		D	NS
Lauroy[133]	1994	A	9
Ramos[134]	1994	C	NS
		C	NS
		C	NS
Cohen[135]	1994	B	3
		B	6
		C	6
		C	9
		C	12
Jacquet[136]	1995	B	10
		B	9
Montorsi[137]	1995	B	2

Table 15 Case reports on port site metastasis

NS = not stated

Early reports of port site metastases after laparoscopic resection of colonic cancer generated considerable concerns in the surgical community in the early 90's such that the initial enthusiasm for the approach was replaced by skepticism. Abdominal wall recurrence after open colectomy was considered to be rare, around 0.7 % based on a retrospective study by Hughes et al [138] despite the study of Cass that reported abdominal wall recurrence in 2.5 % of patients after open resection of colonic cancer [139]. Gunderson et al. showed that two-third of abdominal wall recurrences are missed by physical examination of the abdominal wall[140]. At second look laparotomy 3 months after open curative resection of colonic cancer, 3.3 % of patients had recurrence in the abdominal wall. In the published literature on laparoscopic resection of colonic cancer before 1995, high incidences of port site metastasis were reported, ranging from 0.6 to 21%[132, 141-143]. In a review of data from reports on laparoscopic resection of colonic cancer published later, a much lower rate of 0.85% was recorded by the analysis of 1.769 operations[144]. 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 Table 14 and 15.

Statement 23: Port site metastasis

	Level of evidence	Recommendation
The incidence of port site metastases after laparoscopic colectomy is 1 % or less.	2c	-

7 QUALITY OF LIFE

7.1 Quality of life (standardized questionnaires)

Health-related quality of life associated with laparoscopic colon resection for malignancy has been addressed by few authors[58]. The investigators used the Symptoms Distress Scale, Quality of Life Index (QLI) and a global rating scale. The only statistically significant difference reported ($p=0.009$) was the global rating scale score 2 weeks postoperatively. 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 pronounced early on after surgery.

8 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 multi center RCTs. In the CLASSICC[145], COST[146] and COLOR[147] trials, cost-effectiveness of the two approaches is being evaluated. However, such health economic studies across countries are difficult as data derived from one country cannot be extrapolated to another country due to marked differences in reimbursement and health care systems. Each country should therefore perform its own analysis. Costs used in such analysis include direct costs (costs primarily associated with treatment) and indirect costs (costs secondarily related to disease or treatment).

8.1 Direct costs

Study	Design	direct costs								Indirect costs		
		N lap / open	OR time lap	Instru ments Lap	hospital stay lap	ICU stay Open	Wound complications	radiolo gy	lab	over head Lap	total lap	return to work
Philipson[148]	Retrospective	28 / 33	lap	Lap	lap	Open					lap	
Musser[149]	Case control (historical)	24 / 24	lap	Lap	open			open	open		open	
Kohler[95]	Non randomized prospective	93 / 48	lap	Lap	open		open				open	open

Table 16: comparison of direct and indirect costs in laparoscopic and open resection of colorectal cancer

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. Costs were only collected from the time of surgery until the time of discharge and thus reflected only hospital costs. This study reported higher direct costs of LAC than open hemicolectomy due to increased operating time and the use of disposables [148]. A review on 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 a lower total hospital costs for laparoscopic colectomy [149]. This evaluation included surgery 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 [95]. However, this large study included operations for both benign and malignant colorectal disease and violated the 'intention to treat' principle.

8.2 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 LAC.

8.2.1 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. No study has addressed these costs.

8.3 Cost-effectiveness

For policy making and implementation of new techniques one must assess both costs associated with this technique as well as effects of this technique and its widespread safe applicability. Survival is the most important end point after resection of colonic cancer. 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

	Level of evidence	Recommendation
Operation costs of laparoscopic resection of colonic cancer are higher because of a longer operating time and the use of more expensive (disposable) devices.	3b	-

9 POSTOPERATIVE STRESS RESPONSE*9.1 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 implantation of tumor cells to the traumatized tissues. In general, open surgery appears to inflict a greater non-specific 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[150, 151] and their intrinsic function (phagocytosis)[152, 153] diminishes upon 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[154, 155], production of cytokines[156] and expression of HLA-DR receptors[154, 157] have confirmed this.

9.2 Stress response during colectomy

It has been suggested that survival may be improved if immunosuppression induced by surgery could be reduced or eliminated [158]. The acute-phase response is a good index of the immune status of patients. Production of acute-phase proteins by hepatocytes often increases thousand-fold, as does C-reactive protein (CRP) after tissue injury. This reaction of liver cells is induced by corticoids and cytokines, of which interleukin-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 CRP and IL-6.

Study	Result			Significance	Remarks
	Preoperative	Lap	Open		
1-2					
Ordemann [157]	n.a.	significantly <u>lower</u> after laparoscopy		P < 0.01	Colorectal resection Rand. clin. Trial
Schwenk[159]	4.25 (3.4-7.7)	34.0 (25.6-48.7)	50.5 (39.8-75.7)	P = 0.03	Colorectal resection Clinical trial
Hewitt[90]	n.a.	173 (sd 156)	313 (sd 294)	P = 0.25	Colorectal resection Rand. clin. Trial
Wu[160]	n.a.	83 ± 7	105 ± 33	P < 0.05	Colonic resection Rand. clin. Trial
3					
Sietses [161]	1.75 ± 1.64	85.6 ± 82.3	132.1 ± 143.8	NS	Sigmoid colectomy Non randomized, clinical trial
Fukushima[92]	n.a.	significantly <u>higher</u> after laparoscopy		P < 0.05	Sigmoid colectomy Non randomized, clinical trial
Delgado[162]	n.a.	239.5 (49.1-645.7)	372.7 (31.4-3,226)	P < 0.05	Colectomy Non randomized, clinical trial
Nishiguchi[163]	n.a.	significantly <u>lower</u> after laparoscopy		P < 0.05	Colorectal resection Non randomized, clinical trial
Kuntz [164]	~ 200	287 ± 180	517 ± 208	P = 0.015	Ascending colon resection Rat model

Table 17 Measurements of plasma interleukin-6 levels (IL-6) in pg/ml.

n.a. = not available, NS = not significant, pg/ml = picogram per milliliter

One study reported a significant raise in IL-6 serum level after laparoscopic sigmoid colectomy compared with open conventional surgery. Other studies demonstrated lower IL-6 levels after laparoscopic colorectal resection. Although IL-6 was lower after laparoscopic colectomy, other studies have shown conflicting CRP data (see Table 18).

Study	Results				
	Preoperative	Lap	Open	Significance	Remarks
1-2					
Schwenk [159]	n.a.	40 (33.0-49.4)	61.2 (52.0-77.9)	P = 0.002	Colorectal resection
Wu [160]	n.a.	n.a.	n.a.	NS	Colectomy
3					
Fukushima[92]	n.a.	n.a.	n.a.	NS	Sigmoid colectomy
Delgado [162]	n.a.	6.9 +- 4.5	9.1 +- 4.8	P = 0.01	Colectomy
Nishiguchi [163]	n.a.	Significantly lower after laparoscopy		P < 0.05	Colorectal resection

Table 18 Measurements of plasma C-reactive protein (CRP) in mg/dl.

n.a. = not available, NS = not significant, mg/dl = milligram per deciliter

In addition to cytokines, other cell-related parameters, like delayed type hypersensitivity (DTH) and CD4/CD8 markers have been assessed after laparoscopic colectomy with no significant changes reported between laparoscopic and open colorectal surgery[90, 165].

Statement 25: Stress response

	Level of evidence	Recommendation
Stress response after laparoscopical colectomy is lower.	1b	-

10 SUMMARY OF ALL STATEMENTS AND RECOMMENDATIONS

	Nr.	Statements and recommendations	Level of evidence	Grade of recommendation
		PREOPERATIVE EVALUATION AND SELECTION OF PATIENTS		
<i>Recommendation</i>	1	Preoperative imaging studies of colonic cancer to assess the size of the tumor, possible invasion of adjacent structures, and localization of the tumor are recommended in laparoscopic surgery for colonic cancer.	5	Grade D
<i>Statement</i>	2	Age only is not a contra-indication for laparoscopic resection of colonic cancer.	2b	-
<i>Recommendation</i>	3	Invasive monitoring of blood pressure and blood gases is mandatory in ASA III-IV patients (No consensus: 91% agreement among experts)		Grade A
<i>Recommendation</i>		Low pressure (lower than 12 mm Hg) pneumoperitoneum is advocated in ASA III –IV patients		Grade B
<i>Statement</i>	4	Obesity is not an absolute contra-indication but the rates of complications and conversions are higher at BMI greater than 30 (No consensus: 93% agreement among experts).	2c	-
<i>Recommendation</i>	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
<i>Statement</i>	6	Adhesions are not a contra-indication to laparoscopic colectomy.	4	-
		OPERATIVE TECHNIQUE		
<i>Statement</i>	7	Placement of trocars is based on the experience and the preference of the individual surgeon.	5	-
<i>Recommendation</i>	8	High quality videoscopic imaging and instrumentation is strongly recommended.	5	Grade D
<i>Statement</i>	9	Proper surgical technique and practice reduces the likelihood of port site metastasis.	3a	-
<i>Recommendation</i>	10	Preoperative tattooing of small colonic tumors is advised. The alternatives are intraoperative colonoscopy, or pre-operative colonoscopic clipping followed by peroperative fluoroscopy or ultrasonography. Peroperative ultrasonography can be employed as well at the hands of experts.	5	Grade D
<i>Recommendation</i>	11	Dissection of the mesocolon from medial to lateral is the preferred approach in laparoscopic colonic surgery. During hand-assisted laparoscopic surgery for colonic cancer, the mesocolon can also be resected from lateral to medial.	5	Grade D

	Nr.	Statements and recommendations	Level of evidence	Grade of recommendation
		INTRAOPERATIVE RESULTS OF LAPAROSCOPIC RESECTION OF COLONIC CANCER		
<i>Statement</i>	12	Laparoscopic colectomy is converted to open surgery in % (0 – 42%). The most common causes of conversion are tumour invasion of adjacent structures or bulky tumor, adhesions and technical failure.	3a	-
<i>Statement</i>	13	Laparoscopic colectomy requires more operating time than open colectomy.	2a	-
<i>Statement</i>	14	The extent of laparoscopic lymphadenectomy and bowel resection is similar to those obtained by open colectomy.	2b	-
		CLINICAL OUTCOME		
<i>Statement</i>	15	Morbidity after laparoscopic colectomy does not differ from that after open colectomy.	2b	-
<i>Statement</i>	16	Mortality of laparoscopic colectomy appears similar to that of open colectomy.	2b	-
<i>Statement</i>	17	Hospital stay after laparoscopic resection of colonic cancer is shorter than after open colectomy.	1b	-
<i>Statement</i>	18	Pain is less severe after laparoscopic colectomy.	2a	-
<i>Statement</i>	19	Less analgesia is needed after laparoscopic colectomy compared to open colectomy.	1b	-
<i>Statement</i>	20	Gastro-intestinal function recovers earlier after laparoscopic	2b	-
<i>Statement</i>	21	Postoperative pulmonary function is less impaired after laparoscopic compared to open resection of colonic cancer.	1 or 2b	-
<i>Statement</i>	22	No differences of survival between open and laparoscopic resection of colonic cancer have been reported so far. However, data are insufficient to detect clinically important differences of survival between open and laparoscopic colectomy, if such differences existed.	3b	-
<i>Statement</i>	23	The incidence of port site metastases after laparoscopic colectomy is 1 % or less.	2c	-
		COSTS		
<i>Statement</i>	24	Operation costs of laparoscopic resection of colonic cancer are higher because of a longer operating time and the use of more expensive (disposable) devices.	3b	-
		POSTOPERATIVE STRESS RESPONSE		
<i>Statement</i>	25	Stress response after laparoscopic colectomy is lower.	1b	-

11 REFERENCES

EN.REFLIST