Laparoscopic versus open surgery for the treatment of colorectal cancer: a literature review and recommendations from the Comité de l'évolution des pratiques en oncologie

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Background: Adoption of the laparoscopic approach for colorectal cancer treatment has been slow owing to initial case study results suggesting high recurrence rates at port sites. The use of laparoscopic surgery for colorectal cancer still raises a number of concerns, particularly with the technique's complexity, learning curve and longer duration. After exploring the scientific literature comparing open and laparoscopic surgery for the treatment of colorectal cancer with respect to oncologic efficacy and short-term outcomes, the Comité de l'évolution des pratiques en oncologie (CEPO) made recommendations for surgical practice in Quebec.

Methods: Scientific literature published from January 1995 to April 2012 was reviewed. Phase III clinical trials and meta-analyses were included.

Results: Sixteen randomized trials and 10 meta-analyses were retrieved. Analysis of the literature confirmed that for curative treatment of colorectal cancer, laparoscopy is not inferior to open surgery with respect to survival and recurrence rates. Moreover, laparoscopic surgery provides short-term advantages, including a shorter hospital stay, reduced analgesic use and faster recovery of intestinal function. However, this approach does require a longer operative time.

Conclusion: Considering the evidence, the CEPO recommends that laparoscopic resection be considered an option for the curative treatment of colon and rectal cancer; that decisions regarding surgical approach take into consideration surgeon experience, tumour stage, potential contraindications and patient expectations; and that laparoscopic resection for rectal cancer be performed only by appropriately trained surgeons who perform a sufficient volume annually to maintain competence.

Contexte : L'adoption de la laparoscopie pour traiter le cancer colorectal se fait lentement à cause des résultats des premières études de cas qui indiquent des taux élevés de récidive aux sites d'intervention. La laparoscopie pour traiter le cancer colorectal soulève toujours de nombreuses préoccupations, particulièrement en raison de la complexité de la technique, de la courbe d'apprentissage, et de la durée de la chirurgie. Après avoir étudié des publications scientifiques comparant l'efficacité oncologique et les résultats à court terme de la laparoscopie à ceux de la chirurgie ouverte pour le traitement du cancer colorectal, le Comité de l'évolution des pratiques en oncologie (CEPO) a formulé des recommandations pour la pratique chirurgicale au Québec.

Méthodes : Une revue des écrits scientifiques publiés entre janvier 1995 et avril 2012 a été effectuée. Seuls les essais cliniques de phase III et les méta-analyses ont été répertoriés.

Résultats : Seize essais randomisés et 10 méta-analyses ont été retenus. L'analyse des publications a confirmé que pour le traitement curatif du cancer colorectal, la laparoscopie n'est pas inférieure à la chirurgie ouverte pour ce qui est des taux de survie et de récidive. La laparoscopie offre de plus des avantages à court terme, y compris une hospitalisation de moins longue durée, une réduction de l'usage d'analgésiques et un rétablissement plus rapide de la fonction intestinale. Cette intervention prend toutefois plus de temps.

Conclusion: Compte tenu des données probantes, le CEPO recommande d'envisager la résection laparoscopique comme technique curative possible du cancer colorectal et que les décisions sur la méthode chirurgicale tiennent compte de l'expérience du chirurgien, du stade de la tumeur, des contre-indications possibles et des attentes du patient. Dans le cas de la résection laparoscopique du cancer du rectum, le CEPO recommande qu'elle ne soit pratiquée que par des chirurgiens ayant reçu la formation nécessaire et qui pratiquent suffisamment d'interventions par année pour maintenir leur compétence.

Colorectal cancer is the third most commonly diagnosed cancer and the second leading cause of cancer-related death in Canada. The Canadian Cancer Society estimated that approximately 23 800 new colorectal cases will be diagnosed in Canada in 2013 (6300 in Quebec), and that 9200 related deaths will be reported (2450 in Quebec).[1]

Surgery is the only curative treatment for colorectal cancer. Curative surgery requires resection of the primary tumour with negative margins and a complete oncologic lymphadenectomy. The resected colic segment depends on vascularization and lymphatic drainage at the tumour site and, according to the American Joint Committee on Cancer, a minimum of 12 lymph nodes should be retrieved in surgical specimens. Otherwise, tumour stage could be underestimated, and a suboptimal treatment could be offered.[2]

The surgical approach for rectal cancer is affected by tumour stage and localization.[3] Generally, 5 types of resection can be performed: local excision of the tumour, anterior resection of the rectum, proctectomy with coloanal anastomosis or with terminal colostomy (Hartmann), and abdominoperineal resection. A major improvement in surgical technique was achieved in 1982 when total mesorectal excision was first described and resulted in a substantial reduction in recurrence rates.[4]

Traditionally, colorectal cancer resection has been performed exclusively through open surgery. However, following successful laparoscopic procedures, such as cholecystectomy, appendectomy and treatment of incisional hernias, this surgical approach has gradually been introduced first in the treatment of colon cancer and then in the treatment of rectal cancer.[5] Surgical preparation for laparoscopy is similar to that for open surgery. However, small lesions need to be carefully localized preoperatively by means of colonoscopy (with a tattoo or clip) or barium enema. Laparoscopic resection should result in the removal of the colon or rectal segment containing the tumour and associated lymphatic drainage to the same extent as open surgery. Surgery can be performed entirely by laparoscopy, be laparoscopy-assisted (anastomosis is then performed extracorporally) or be hand-assisted (in which case a sufficiently long incision is made to allow the surgeon's hand to enter the abdominal cavity). For all 3 strategies, the abdominal wall incision should be protected to prevent tumour dissemination.[6]

Laparoscopic resection of the sigmoid colon was first described by Jacobs and colleagues[7] in 1991. However, generalized adoption of the laparoscopic procedure was slower for colorectal cancer than for other pathologies. This can be explained by the disappointing results of initial case studies on laparoscopic colon cancer resection, which revealed high recurrence rates at port sites.[8,9] Despite the fact that more recent studies did not reproduce these results,[10,11] many concerns still persist about the use of laparoscopic surgery in colon and rectal cancer treatment, notably with respect to the technique's complexity, the associated learning curve and the longer operative time.[5]

About half the general surgeons in Canada perform laparoscopic colorectal surgery. The highest rate of adoption of laparoscopic surgery is in Quebec, where it is estimated at 67%. Significant predictors for offering a laparoscopic approach are recent graduation, male sex, province of practice, university affiliation and minimally invasive surgery training, whereas constraints for adoption of this technique include the lack of available operative time and lack of formal training programs.[12]

The present review explores the relevant scientific literature comparing open and laparoscopic surgery in the treatment of colon and rectal cancer with respect to oncologic efficacy and short-term risks and benefits. Based on the best available evidence, recommendations have been made for surgical practice in Quebec.

Methods

Published clinical trials comparing open and laparoscopic surgery in colon and rectal cancer treatment were retrieved using the medical subject headings "colorectal neoplasms," "rectal neoplasms," "general surgery," "colorectal surgery," "laparoscopy" and "colectomy" as well as the keywords "colorectal cancer," "colon cancer," "rectal neoplasms," "rectal cancer," "open surgery," "resection," "laparoscopy," "colectomy," "rectal surgery" and "total mesorectal excision." Only English- and French-language phase III randomized trials and meta-analyses were selected. Specifically for colon cancer, in light of the large number of studies retrieved and the variations in study quality, only trials involving more than 200 patients were retained. The period covered was from January 1995 to April 2012, inclusively. Studies reporting data on colorectal cancer were considered only if specific data on colon and rectal cancer were presented separately. Economic studies, trials pertaining to metastatic disease of the colon or rectum and trials addressing chemotherapy- or radiotherapy-based treatments were excluded. Abstracts presented at the American Society of Clinical Oncology (ASCO) and European Society for Medical Oncology (ESMO) meetings from 2008 to 2012 were also reviewed, and only those reporting phase III trial results were included.

The level of evidence of selected studies and the strength of recommendation were evaluated using the ASCO and ESMO gradation system (Table 1).[13] The original guideline was developed by a CEPO subcommittee, reviewed by independent experts and, finally, adopted by the CEPO by consensus.

Results

Eight phase III randomized clinical trials[10,11,14–27] and 5 meta-analyses[28–32] comparing laparoscopy and open

Table 1. Levels of evidence and grades of recommendations

Level or grade	Description
Level of evidence	
I	Evidence demonstrated by means of meta-analyses of well-designed controlled trials or large randomized trials with clear-cut results (low rate of false-positive and false-negative errors, high power)
II	Evidence demonstrated by means of small randomized trials with uncertain results (high rate of false-positive and false-negative errors, low power)
III	Evidence demonstrated by means of nonrandomized concurrent cohort comparisons with contemporaneous controls
IV	Evidence demonstrated by means of nonrandomized historical cohort comparisons
V	Evidence demonstrated by means of case series without controls
Grade of recommendation	
A	Supported by Level I evidence or multiple Level II, III or IV trials presenting concordant observations
B	Supported by Level II, III or IV trials presenting generally concordant observations
C	Supported by Level II, III or IV trials presenting nonconcordant observations
D	Supported by few trials or no empiric evidence

Adapted from Cook and colleagues[13] with permission from the American College of Chest Physicians.

Table 2. Main characteristics of randomized clinical trials on colon cancer

Variable	COLOR[10,14]	COST[16,17]	CLASICC[11,20,21]*	LAPKON II[26]	ALCCaS[27]	Barcelona[22,23]	Liang[24]	LAFA-study[25]†
Study design, Phase III	multi	multi	multi	multi	multi	single	single	multi
Concealment	Computer-generated random numbers	Centralized	Centralized by telephone	Centralized by telephone Revealed during operation	Centralized	Sealed envelopes	Random-sized blocks 2–10	2 × 2 Internet randomization module
Median follow-up, mo.	53	60	37	§	§	43	40	—
Primary outcomes	3-year DFS	Time to recurrence	3-year DFS 3-year OS LR	§	§	Cancer-related survival	Time to recurrence	Total postop hospital stay
Level of evidence‡	I	I	I	I	I	II	II	I
Population, no								
OP	542	428	140	222	298	102	134	108
LAP	534	435	273	250	294	106	135	110
Tumour stage								
I	24%	26% (OP) 35% (LAP)	NA	28% (OP) 35% (LAP)	23%	22%	—	NA
II	43%	34% (OP) 31% (LAP)	NA	38% (OP) 32% (LAP)	40%	43%	49%	NA
III	33%	28% (OP) 26% (LAP)	NA	33% (OP) 33% (LAP)	30%	35%	51%	NA
IV	—	4% (OP) 2% (LAP)	NA	—	2%	—	—	NA
Postoperative chemotherapy	According to surgeon (p = 0.99)	According to surgeon	29% (OP) 28% (LAP)	NA	NA	55% (OP) 61% (LAP)	For stage III patients	NA
Surgery								
Surgical procedure								
Right	47%	54%	45%	29%	58%	45%	—	48%
Left	11%	7%	13%	¶	4%	2%	70%	49%
Sigmoid	38%	38%	21%	¶	—	45%	30%	—
Anterior	—	—	11%	—	38%	5%	—	—
Conversion rate	19%	21%	25%	11%	15%	11%	3%	11%
Surgeon experience	≥ 20 LAP colectomies	≥ 20 LAP colectomies	≥ 20 LAP resections	≥ 20 LAP colectomies	52% surgeons treated > 10 patients	Experienced team	Experienced surgeon	≥ 20 LAP for benign disease

CLASICC = Conventional Versus Laparoscopic-Assisted Surgery in Patients with Colorectal Cancer; COLOR = Colon Cancer Laparoscopic or Open Resection; COST = Clinical Outcomes of Surgical Therapy; DFS = disease-free survival; LAP = laparoscopy; LR = local recurrence; multi = multicentred; NA = not available; OP = open surgery; OS = overall survival; single = single-centred.

*This trial included patients with colon and rectum cancers. When available, only data specific to colon cancer are presented.

†This trial evaluated fast-track versus standard care and LAP versus OP (4 arms). Only the 2 arms with standard care (LAP v. OP) are presented.

‡As evaluated according to the American Society of Clinical Oncology and European Society for Medical Oncology gradation system (see Table 1).

§Only short-term outcomes are published.

¶71% for left plus rectosigmoid.

surgery for the treatment of colon cancer were identified. For rectal cancer, 9 phase III randomized clinical trials[11,20,21,33–42] and 7 meta-analyses were selected.[28,29,43–47] No meeting abstracts satisfied the inclusion criteria. The main design characteristics of each randomized trial are summarized in Table 2 for colon cancer and in Table 3 for rectal cancer.

Oncologic outcomes: colon cancer

Phase III randomized trials

In 2009, Buunen and colleagues[10] presented the long-term results of the Colon cancer Laparoscopic or Open Resection (COLOR) noninferiority trial. The primary outcome was 3-year disease-free survival, which was 74.2% with the laparoscopic procedure and 76.2% with open surgery. Noninferiority thresholds were set at a 7% difference between the 2 procedures at a level of significance of p = 0.025. These 2 criteria were not met, since the superior limit of the 95% confidence interval (CI) of the observed difference reached 7.2% (p = 0.03). Three-year overall survival was 81.8% after laparoscopy and 84.2% after open surgery (p = 0.45).

In 2004, the long-term results of the Clinical Outcomes of Surgical Therapy (COST) noninferiority trial[16] were presented. The cut-offs to declare the laparoscopic procedure noninferior to open surgery regarding time to recurrence at 3 years were set at a hazard ratio (HR) of less than 1.23 and $p \geq 0.41$. According to these criteria, the laparoscopic procedure was not inferior to open surgery (p = 0.83). The cumulative incidence of recurrence did not significantly differ between the 2 procedures (HR 0.86, 95% CI 0.63–1.17, p = 0.32). No differences in overall survival (HR 0.91, 95% CI 0.68–1.21, p = 0.51) or disease-free survival (HR 0.95, 95% CI 0.74–1.23, p = 0.70) were observed. In 2007, Fleshman and colleagues[17] published updated results after 5 years of follow-up and confirmed the noninferiority of laparoscopy in terms of time to recurrence

Table 3. Main characteristics of randomized clinical trials on rectal cancer

Variable	Liang[33]	COREAN[34]	CLASICC[11,20,21]*	Lujan[36]	Ng[37,38]	Ng[39]	Pechlivanides[40]	Braga[41]*	Zhou[42]
Study design, Phase III	single	multi	multi	single	single	single	multi	single	single
Concealment	Opaque envelopes	Computer-generated	Centralized, by phone	Computer-generated	Computer-generated	Computer-generated	Computer-generated	Computer-generated	NA
Median follow-up, mo.	44	NA	37	34 (OP) 33 (LAP)	113 (OP) 109 (LAP)	91 (OP) 87 (LAP)	NA	54	NA
Primary outcomes	3-year OS	DFS	5-year DFS, 5-year OS, LR	No. lymph nodes retrieved, integrity of mesorectal resection margin	Long-term morbidity	Postoperative recovery	No. lymph nodes retrieved	Short-term postopmorbidity	Short-term results
Level of evidence†	I	I	I	I	I	I	I	I	I
Population, no									
OP	174	170	128	103	77	48	39	89	89
LAP	179	170	253	101	76	51	34	82	82
Tumour stage									
I	NA	NA	NA	15% (OP) 11% (LAP)	15% (OP) 17% (LAP)	NA	NA	NA	NA
II	NA	NA	NA	38% (OP) 35% (LAP)	38% (OP) 38% (LAP)	NA	NA	NA	NA
III	NA	NA	NA	43% (OP) 45% (LAP)	26% (OP) 36% (LAP)	NA	NA	NA	NA
IV	NA	NA	NA	5% (OP) 10% (LAP)	21% (OP) 9% (LAP)	NA	NA	NA	NA
Postoperative chemotherapy	NA	Recommended for 4 mo	29% (OP) 28% (LAP)	Stage III or IV disease	33% (OP) 14% (LAP)	NA	NA	NA	NA
Surgery									
Tumour distance from AV, cm	NA	5.3 (OP) 5.6 (LAP)	NA	6.2 (OP) 5.5 (LAP)	12–15 cm	≥ 5 cm	8 (OP) 6 (LAP)	8.6 (OP) 9.1 (LAP)	NA
Conversion rate	< 1%	1%	34%	8%	30%	10%	3%	7%	NA
Surgeon experience	Experienced surgeon	28–150 LAP	≥ 20 LAP	Experienced team	Experienced surgeon	Experienced surgeon	Experienced surgeon	Experienced team	Experienced surgeon

AV = anal verge; CLASICC = Conventional Versus Laparoscopic-Assisted Surgery in Patients with Colorectal Cancer; COREAN = Comparison of Open versus laparoscopic surgery for mid and low Rectal cancer After Neoadjuvant chemoradiotherapy; DFS = disease-free survival; LAP = laparoscopy; LR = local recurrence; NA = not available; OP = open surgery; OS = overall survival.
*This trial included patients with colon and rectum cancers. When available, data specific to rectal cancer are presented.
†As evaluated according to the American Society of Clinical Oncology and European Society for Medical Oncology gradation system (Table 1).

(p = 0.75) and cumulative incidence of recurrence (HR 0.84, 95% CI 0.62–1.13, p = 0.25).

In 2007, Jayne and colleagues[11] presented the long-term results of the Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer (CLASICC) trial. The objective was to assess overall survival, disease-free survival and local recurrence at 3 years in patients with colon or rectal cancer treated with laparoscopic or open surgery. For colon cancer, the local recurrence rates were 7.3% with laparoscopy and 6% with open surgery (p = 0.68). Differences between the 2 approaches with respect to 3-year overall survival (p = 0.51) and disease-free survival (p = 0.75) were not significant. Updated data showed similar results between groups assigned to laparoscopy and open surgery for 5-year overall survival (55.7% v. 62.7%, p = 0.25) and disease-free survival (57.6% v. 64%, p = 0.40).[20]

In 2008, Lacy and colleagues[22] presented long-term results of a phase III randomized trial conducted in Barcelona, Spain, updating data initially published in 2002.[23] The primary outcome was cancer-related mortality. After 3.5 years of follow-up, cancer-related mortality was 9% with laparoscopy and 21% with open surgery (p = 0.03); after a median follow-up of 8 years, the rate was 16% and 27%, respectively, (p = 0.07). Recurrence rates of 18% with laparoscopy and 28% with open surgery were also observed (p = 0.07).

In 2007, Liang and colleagues[24] published results of a randomized trial conducted in Taiwan by a single surgeon. Time to recurrence after colon cancer resection was not significantly different between the laparoscopic and open procedure (p = 0.36). The cumulative incidence of recurrence was 17% with laparoscopy and 21.6% with open surgery.

In 6 trials, the extent of resection, as measured by resection margins and the number of lymph nodes harvested, did not significantly differ between laparoscopic and open surgery. The number of lymph nodes harvested varied between 10 and 17.[14,16,21,23,24,26] In the studies reporting recurrence rates at wound or port sites, the rates were not statistically different between the groups (1.3% v. 0.4%, p = 0.09;[10] 0.9% v. 0.5%, p = 0.43;[17] 0.9% v. 0%, p value not available;[23] and 0.7% v. 0.7%, p value not available,[24] for the laparoscopic and open procedures, respectively).

Meta-analyses

In 2011, Ma and colleagues[29] conducted a meta-analysis comparing laparoscopy with open resection for colorectal cancer. Data from 6 studies (n = 1800) specific to colon cancer showed that cancer-related mortality was 17.7% with laparoscopy and 19.7% with open surgery (odds ratio [OR] 0.85, 95% CI 0.66–1.09, p = 0.20).

In 2010, Bai and colleagues[30] conducted a meta-analysis including 3 trials (n = 2147)[10,17,22] that reported long-term outcome data following laparoscopic and open colon resection. Overall mortality was similar for laparoscopy and open surgery (24.9% v. 26.4%, OR 0.92, 95% CI 0.76–1.12, p = 0.41). Overall recurrence rates of 19.3% and 20% (OR 0.96, 95% CI 0.78–1.19, p = 0.71), local recurrence rates of 4% and 4.4% (OR 0.91, 95% CI 0.59–1.39, p = 0.66) and distal recurrence rates of 12.8% and 14% (OR 0.90, 95% CI 0.70–1.16, p = 0.41) were also observed with laparoscopic and open surgery, respectively.

In 2008, Kuhry and colleagues[31] conducted a Cochrane collaboration meta-analysis comparing survival and recurrence rates in patients with colorectal cancer treated with laparoscopic or open surgery. This meta-analysis included 12 trials. Four trials (n = 938) presented results of recurrence in patients with colon cancer. The local recurrence rate was 5.2% with laparoscopic surgery and 5.6% with open resection (OR 0.84, p = 0.57), whereas distant recurrence was 11.3% and 13.6%, respectively (OR 0.82, p = 0.32). In 5 trials (n = 1575), cancer-related mortality was 14.6% with laparoscopy and 16.4% with open surgery (OR 0.80, p = 0.12). The combined results of 4 trials (n = 1162) showed overall mortality of 20.4% with laparoscopy and 23.6% with open surgery (OR 0.82, p = 0.17).

In 2007, Bonjer and colleagues[32] presented a meta-analysis combining individual data on patients recruited before March 2000 in the COLOR, COST, CLASICC and Barcelona trials (n = 1536). The 3-year overall survival (82.2% v. 83.5%, p = 0.56) and disease-free survival (75.8% v. 75.3%, p = 0.83) were similar between laparoscopic and open colectomy, respectively.

A recent meta-analysis[28] showed that the number of lymph nodes harvested was similar with laparoscopic and open colon resection (weighted mean difference [WMD] –0.18, p = 0.82).

Oncologic outcomes: rectal cancer

Phase III randomized trials

In 2011, Liang and colleagues[33] presented results of a randomized trial conducted in a single centre in China to evaluate 3-year overall survival following laparoscopic or open surgery for rectal cancer. After a median follow-up of about 44 months, overall survival was similar for laparoscopic and open surgery (76% v. 82.8%, p = 0.46). There was no difference between these 2 procedures in the median number of lymph nodes harvested (7.1 v. 7.4, p = 0.47) or the distance between the inferior border of the tumour and the incised margin in the lower anterior resection operation (3.2 cm v. 3.1 cm, p = 0.15).

In 2010, Kang and colleagues[34] presented the short-term oncologic results of the Comparison of Open versus laparoscopic surgery for mid and low REctal cancer After Neoadjuvant chemoradiotherapy (COREAN) trial. The tumour had to be localized at no more than 9 cm from the anal verge. No difference was shown between laparoscopic and open surgery with respect to the macroscopic quality of the resected mesorectum (complete 72.4% v. 74.7%;

almost complete 19.4% v. 13.5%; incomplete 4.7% v. 6.5%; $p = 0.41$), the median number of lymph nodes harvested (17 v. 18, $p = 0.09$), the negative circumferential margins (97.1% v. 95.5%, $p = 0.77$) and the rate of negative proximal, distal and radial margins ($p = 0.44$, $p = 0.54$ and $p = 0.31$, respectively).

In 2010, Jayne and colleagues[20] presented updated results of the CLASICC trial after a median follow-up of 56.3 months. For rectal cancer, overall survival (60.3% v. 52.9%, $p = 0.13$) and disease-free survival (53.2% v. 52.1%, $p = 0.95$) were similar for laparoscopic and open surgery, respectively. No difference was observed between laparoscopic and open procedures in local and distal recurrence rates. Distal recurrence rates were 21.9% with both laparoscopic and open anterior resection, whereas they were 35.7% with laparoscopic abdominoperineal resection and 40.8% with open abdominoperineal resection. Local recurrence rates were 9.4% with laparoscopic and 7.6% with open anterior resection. Positive resection margins were more frequent with laparoscopic than open anterior resection (12.4% v. 6.3%, $p = 0.01$), but not with abdominoperineal resection (20% v. 26%, p value not available).

In 2009, Lujan and colleagues[36] presented results of a noninferiority randomized trial that evaluated efficacy of laparoscopy compared with open resection of the low or mid rectum. Five-year disease-free survival (84.8% v. 81%, $p = 0.90$), overall survival (72.1% v. 75.3%, $p = 0.98$) and local recurrence (4.8% v. 5.3%, $p = 0.78$) were similar with laparoscopic and open surgery, respectively. The mean number of lymph nodes harvested was greater with laparoscopy than with open surgery (13.6 v. 11.6, $p = 0.03$). Integrity of the resection margins was similar with laparoscopic and open procedures (2.8% v. 4%, $p = 0.42$).

In 2009, Ng and colleagues[37] presented results of a randomized trial conducted in a single centre in Hong Kong to evaluate long-term oncologic efficacy of laparoscopic surgery for proximal rectal cancer (12–15 cm from the anal verge). After a median follow-up of about 110 months, no difference was found between laparoscopic and open surgery in terms of overall survival ($p = 0.30$), cancer-related survival ($p = 0.60$) and disease-free survival ($p = 0.70$) in patients with stage I–III rectal cancer. Mean survival was not different for stage IV cancer ($p = 0.16$). During the 10-year follow-up period, 37.3% of patients assigned to laparoscopy and 38.8% of patients assigned to open surgery died; 15.3% and 16.4% were rectal cancer-related deaths, and 18.6% and 19.4% were other cancer-related deaths, respectively. Recurrence rates (local 7.1% v. 4.9%, $p = 0.68$; distal 12.3% v. 18.1%, $p = 0.37$), mean number of lymph nodes harvested (11.5 v. 12, $p = 0.70$) and positive resection margins (2.6% v. 1.3%, $p = 0.62$) were similar with laparoscopic and open surgeries, respectively.

In 2008, Ng and colleagues[39] presented results of a randomized trial conducted in a single centre in Hong Kong that evaluated laparoscopic surgery in distal rectal cancer treatment (up to 5 cm from the anal verge). After a median follow-up of about 90 months, no difference was found between laparoscopic and open surgery for 5-year overall survival (75.2% v. 76.5%, $p = 0.20$) and disease-free survival (78.1% v. 73.6%, $p = 0.55$) in patients with stage I–III rectal cancer. In patients with stage IV disease, mean survival was 32.6 months after laparoscopy and 13.9 months after open surgery ($p = 0.05$). During the follow-up period, 30% of patients assigned to laparoscopy and 47.2% of patients assigned to open surgery died; 15% and 22.2%, respectively, were cancer-related deaths. Recurrence rates were similar with laparoscopic and open surgery ($p = 0.60$), as were the mean number of lymph nodes harvested (12.4 v. 13, $p = 0.72$) and the positive resection margins rate (6.3% v. 3.9%).

In 2007, Pechlivanides and colleagues[40] presented the results of a randomized trial conducted by a single surgeon to compare laparoscopic and open surgeries in the treatment of rectal cancer localized at less than 12 cm from the anal verge. The mean number of lymph nodes harvested was 19.2 in both groups ($p = 0.2$). No data on survival or recurrence were presented.

In 2007, Braga and colleagues[41] presented results of a randomized trial, conducted in Italy by a single team, after a median follow-up of 53.6 months. No difference was observed between groups assigned to laparoscopy or open surgery for 5-year overall survival (stage I: $p = 0.93$, II: $p = 0.37$, III: $p = 0.98$, and IV: $p = 0.95$), 3-year local recurrence (4% v. 5.2%, $p = 0.97$) and mean number of lymph nodes harvested (12.7 v. 13.6, p value not available). The distal margins were negative in all patients whereas positive circumferential margins were observed in 1 patient treated with laparoscopy (1.3%) and 2 patients treated with open surgery (2.4%).

Meta-analyses

In 2011, Huang and colleagues[43] conducted a meta-analysis including 6 clinical trials ($n = 1033$) that evaluated efficacy of laparoscopic surgery in rectal cancer treatment. Three-year overall survival ($p = 0.11$, 4 trials) and disease-free survival ($p = 0.11$, 3 trials) were not significantly different after

Table 4. Comparison of oncologic results in rectal cancer[44]

Result	OR (95% CI)	*p* value
Progression-free survival		
3-year	0.90 (0.66–1.24)	0.53
5-year	1.17 (0.85–1.61)	0.35
Recurrence		
Total	0.93 (0.68–1.25)	0.61
Local	0.83 (0.52–1.31)	0.41
Wound sites	1.34 (0.07–24.10)	0.84
Distal metastasis	0.89 (0.63–1.27)	0.52
Mortality		
Overall	0.80 (0.60–1.07)	0.13
Cancer-related	0.71 (0.45–1.12)	0.14

CI = confidence interval; OR = odds ratio.

laparoscopy or open surgery. After a follow-up ranging from 32.8 to 112.5 months, local recurrence rates after laparoscopic and open surgery were not statistically different (p = 0.21, 4 trials). No difference was observed between laparoscopy and open surgery for the mean number of lymph nodes harvested (p = 0.43, 5 trials); positive circumferential resection margins were also similar (7.9% v. 5.4%, p = 0.63, 5 trials).

In 2011, Ohtani and colleagues[44] conduted a meta-analysis comparing the oncologic efficacy of laparoscopic and open surgery for rectal cancer. Twelve trials were included (n = 2095), and results showed no difference between the 2 procedures for the oncologic outcomes measured (Table 4).

In the meta-analysis comparing laparoscopy with open resection for colorectal cancer by Ma and colleagues[29] in 2011, data specific to rectal cancer from 5 studies were presented (n = 991). Cancer-related mortality was 13.1% with laparoscopy and 15.3% with open surgery (OR 0.76, 95% CI 0.53–1.11, p = 0.16).

In 2008, Anderson and colleagues[45] conducted a meta-analysis including 22 clinical trials that evaluated the efficacy of laparoscopic surgery in rectal cancer treatment. After 4.4 years of follow-up (13 trials), overall survival was 72% with laparoscopy and 65% with open surgery (p = 0.5). At a median follow-up of 35 months, local recurrence rates after laparoscopic and open surgery were 7% and 8%, respectively (16 trials), whereas distal recurrence rates were 12% and 14%, respectively (p = 0.54, 9 trials). The mean number of lymph nodes harvested was lower with laparoscopy than with open surgery (10 v. 12, p = 0.001, 17 trials); however, 3 trials showed that more lymph nodes were harvested with laparoscopy. The rate of positive resection margins was similar with laparoscopic and open surgery (5% v. 8%, 10 trials).

Three additional meta-analyses compared short-term oncologic outcomes after laparoscopic and open surgery for rectal cancer and showed no difference between the procedures in terms of the mean number of lymph nodes harvested and the rate of positive resection margins.[28,46,47]

Short-term outcomes

Duration of operation

Thirteen trials presented data on the duration of surgery for colon and rectal cancer (Table 5). In all but 1 study, operative time was longer for laparoscopic than for open surgery. The COLOR trial investigators showed that differences in operative time between the 2 procedures for colon cancer tended to be smaller in centres with high volumes (p = 0.027).[14]

Intraoperative blood loss

Five trials assessed median intraoperative blood loss during laparoscopic and open surgeries for colon cancer.[10,23–25,27] Four trials observed less blood loss during laparoscopy: COLOR (100 mL v. 175 mL, p = 0.003),[10] Barcelona (105 mL v. 193 mL, p = 0.001),[23] Liang and colleagues[24] (54 mL v. 240 mL, p < 0.001) and LAFA-study (100 mL v. 200 mL, p < 0.001).[25] Only the Australasian Laparoscopic Colon Cancer Study (ALCCaS) trial showed no significant difference between the 2 procedures (median blood loss of 100 mL in both cases, p = 0.17).[27]

Six trials assessed intraoperative blood loss during rectal cancer surgery.[34,36,37,39,41,42] All trials showed a trend toward less blood loss with laparoscopy; this trend was significant

Table 5. Operative time of open and laparoscopic surgeries

	Operative time; median (range) or mean ± SD, min		
Trial	Open surgery	Laparoscopic surgery	p value
Colon cancer			
COLOR[10]	115 (70–180)	145 (102–230)	< 0.001
COST[16]	95 (27–435)	150 (35–450)	< 0.001
Barcelona[23]	118 ± 45	142 ± 52	0.001
Liang et al.[24]	184 ± 31	224 ± 45	< 0.001
LAPKON II[26]	138 ± 45	183 ± 61	< 0.001
ALCCaS[27]	107 (45–250)	158 (49–365)	< 0.001
Rectal cancer			
Liang et al.[33]	119 ± 22	138 ± 24	< 0.001
COREAN[34]	197 ± 63	245 ± 75	< 0.001
Lujan et al.[36]	173 ± 59	194 ± 45	0.020
Ng et al.[37]	154 ± 70	213 ± 59	< 0.001
Ng et al.[39]	164 ± 43	214 ± 46	< 0.001
Braga et al.[41]	209 ± 70	262 ± 72	< 0.001
Zhou et al.[42]	106 (80–230)	120 (110–220)	0.05

ALCCaS = Australasian Laparoscopic Colon Cancer Study; COLOR = Colon cancer Laparoscopic or Open Resection; COREAN = Comparison of Open versus laparoscopic surgery for mid and low Rectal cancer After Neoadjuvant chemoradiotherapy; COST = Clinical Outcomes of Surgical Therapy; SD = standard deviation.

in 4 trials: COREAN (200 mL v. 217.5 mL, $p = 0.006$),[34] Lujan and colleagues[36] (127.8 mL v. 234.2 mL, $p < 0.001$), Braga and colleagues[41] (150 mL v. 350 mL, $p < 0.001$) and Zhou and olleagues[42] (20 mL v. 92 mL, $p = 0.05$).

Two trials compared transfusion use during laparoscopic and open surgeries for the treatment of colon cancer.[26,27] Sixteen patients undergoing laparoscopy (5.4%) versus 18 patients undergoing open surgery (6%) received a transfusion in the ALCCaS trial,[27] whereas 11.6% and 17.6% of patients assigned to laparoscopic and open surgery, respetively, received transfusion in LAPKON II.[26] Three trials evaluated transfusion rates during rectal cancer resection.[33,34,41] Only 1 patient, assigned to open surgery, needed a transfusion in the COREAN trial ($p > 0.99$),[34] whereas 4 patients (2.4%) assigned to laparoscopy and 8 patients (4.6%) assigned to open surgery needed a transfusion in the trial by Liang and colleagues[33] ($p = 0.38$). Braga and colleagues[41] observed transfusion rates of 7.2% with laparoscopy and 26.8% with open surgery ($p = 0.002$).

Postoperative pain

Liang and colleagues[24] measured postoperative pain using a visual analogue scale of 0–10. Less pain was recorded after laparoscopy than open surgery for colon cancer (median 3.5 v. 8.6, $p < 0.001$). In the COREAN trial, mean postoperative pain was less after laparoscopy than open surgery up to 3 days after surgery for rectal cancer ($p < 0.05$).[34] Ng and colleagues[39] reported no difference in pain, according to the visual analogue scale, on the first day after laparoscopic and open surgery for rectal cancer ($p = 0.41$).

In 2 trials, less analgesic use was reported after laparoscopy than open surgery for colon cancer. In the COLOR trial, 8%–14% fewer patients needed analgesics in the first 3 days after laparoscopy than open surgery ($p < 0.001$ to $p = 0.008$).[14] In the COST trial, this difference corresponded to a median of 1 day less needing analgesics.[16] There was also less analgesic use after laparoscopy than open surgery for rectal cancer, according to 4 trials. In these trials, lower doses of morphine (median 107.2 mg v. 156.9 mg, $p < 0.001$),[34] and fewer injections of analgesics (mean 6 v. 11.4, $p = 0.007$ and 4.9 v. 8.3, $p = 0.001$)[37,39] were used by patients assigned to laparoscopy than open surgery. The median duration of analgesic treatment was also shorter (3.9 d v. 4.1 d, $p = 0.23$).[42]

Recovery of intestinal function

For colon cancer, Liang and colleagues[24] found that postoperative ileus lasted for a mean of 48 hours after laparoscopy compared with 96 hours after open surgery ($p < 0.001$). In the Barcelona trial, peristalsis began at a mean of 36 hours after laparoscopic surgery compared with 55 hours after open surgery ($p = 0.001$).[23] In the ALCCaS trial, the mean time to passing first flatus was 3.2 days after laparoscopy compared with 3.5 days after open surgery ($p = 0.027$).[27] Finally, 3 trials measured time to first bowel movement: 3.6, 5.0 and 4.4 days, respectively, after laparoscopy and 4.6, 6.0 and 4.9 days, respectively, after open surgery ($p < 0.001$,[14] p value not available[21] and $p = 0.011$,[27] respectively).

For rectal cancer, peristalsis also began sooner after laparoscopy than open surgery, as found in 5 trials: Liang and colleagues[33] (3.9 d v. 4.2 d, $p < 0.001$), Ng and colleagues[39] (4.3 d v. 6.3 d, $p < 0.001$), Ng and colleagues[37] (4.1 d v. 4.7 d, $p = 0.06$), CLASICC (5 d v. 6 d, p value not available)[21] and Zhou and colleagues[42] (1.5 d v. 2.7 d, $p = 0.009$). This conclusion is supported in a meta-analysis (WMD –1.52 d, 95% CI –2.20 to –1.01).[46] The mean time to passing first flatus was also shorter after laparoscopy (38.5 hr v. 60 hr, $p < 0.001$[34] and 3.1 d v. 4.6 d, $p < 0.001$[39]), as was the mean time for first stool (3 d v. 3.3 d, $p < 0.001$[33] and 96.5 hr v. 123 hr, $p < 0.001$[34]). Return to normal diet after laparoscopic and open surgery for rectal cancer was evaluated in 4 trials: COREAN (85 hr v. 93 hr, $p < 0.001$),[34] Ng and colleagues[39] (4.3 d v. 6.3 d, $p = 0.001$), Ng and colleagues[37] (4.3 d v. 4.9 d, $p = 0.001$) and CLASICC (6 d v. 6 d; p value not available).[21] Faster return to normal diet after laparoscopy was confirmed in a meta-analysis (WMD –0.92 d, 95% CI –1.35 to –0.50).[46]

Length of hospital stay

Seven trials presented data on length of hospital stay after colon cancer surgery (Table 6). In all cases, patients treated with laparoscopy had a shorter hospital stay than patients treated with open surgery. However, the ALCCaS trial showed that among laparoscopy-treated patients, those who were converted to open surgery had a significantly longer hospital stay than those who were not converted (14.6 d v. 8.6 d, $p < 0.001$).[27] As for rectal cancer, 7 trials presented data on length of hospital stay (Table 6). Although all trials reported a shorter hospital stay after laparoscopy than open surgery, the difference was significant in only 3 trials. In addition, a meta-analysis showed that hospital stay was shorter after laparoscopy than open surgery for rectal cancer (WMD –2.67 d, 95% CI –3.81 to –1.54).[46]

Morbidity and mortality

Overall complication rates following colon cancer resection were evaluated in 4 trials. Only in the Barcelona trial was the complication rate lower for laparoscopy than open surgery (11% v. 29%, $p = 0.001$),[23] whereas COLOR,[14] LAFA-study[25] and the study by Liang and colleagues[24] reported no significant difference after laparoscopic or open procedures ($p = 0.88$, $p = 0.20$ and $p = 0.15$, respectively). Reported intraoperative complications included hemorrhage, cardiac or pulmonary insufficiency, adverse anesthetic events and injury of bowel or adjacent organs. The intraoperative complication rate was statistically higher following laparoscopy in 1 trial (10.5% v. 3.7%, $p = 0.001$),[27] whereas 3 trials showed no difference between laparoscopic and open procedures (4% v. 2%, $p = 0.10$,[16] 7% v. 8%, p value not available,[21] and 5.6% v. 2.3%, $p = 0.10$[26]). No difference in postoperative complication rates

was found in these 4 trials between laparoscopic and open surgery (37.8% v. 45.3%, $p = 0.06$,[27] 19% v. 19%, $p = 0.98$,[16] 26% v. 27%, p value not available,[21] and 25.2% v. 23.9%, $p = 0.75$[26]). Wound or urinary tract infections, anastomotic leakage, prolonged ileus, hemorrhage, and various cardiac, pulmonary or vascular complications were the most frequent postoperative complications reported.

Complication rates following rectal cancer resection were presented in 7 trials.[21,34,36,37,39,41,42] The intraoperative complication rates ranged from 6.1% to 21.2% for laparoscopy and from 12.4% to 23.5% for open surgery ($p = 0.016$ to $p = 0.60$),[21,34,42] and the postoperative complication rates ranged from 2.4% to 45.1% and from 10.6% to 52.1%, respectively ($p = 0.012$ to $p = 0.96$).[36,37,39,41] Results of a meta-analysis showed that patients assigned to laparoscopy presented less morbidity than those assigned to open surgery (OR 0.63, 95% CI 0.41–0.96, $p = 0.030$).[47] Reported intraoperative complications included hemorrhage, cardiac or pulmonary insufficiency, anesthesia-related complications and injury of serosa or adjacent organs, whereas postoperative complications included anastomotic leakage, wound and urinary tract infections and various cardiac, pulmonary or vascular complications. Four trials reported the need for reoperation, and none observed any difference between patients undergoing laparoscopic and open surgery for the frequency of second operation.[34,37,39,41]

Six trials reported short-term mortality following laparoscopic or open resection for colon cancer.[10,16,23,25–27] In all of these studies, mortality was 2% or less and was not significantly different between the 2 groups ($p = 0.40$ to $p = 0.99$). Six trials reported the short-term mortality for rectal cancer and showed no difference between laparoscopic and open procedures.[21,33,36,37,39,41] The highest mortality was observed in the CLASICC trial (4% following laparoscopy and 5% following open surgery, $p = 0.57$).

Quality of life

Three trials evaluated quality of life following laparoscopic and open surgery in patients with colon cancer. In a subgoup of the COLOR trial ($n = 285$), social function at 2 ($p = 0.046$), 4 ($p = 0.031$) and 12 ($p = 0.05$) weeks and role function at 2 weeks ($p = 0.006$) were better following laparoscopic than open surgery.[15] In the COST trial ($n = 428$), only the global quality of life score 2 weeks after surgery was higher following laparoscopy (80 v. 75, p value not available),[18] whereas only the global quality of life score ($p = 0.05$) and the subdomain of outlook ($p = 0.02$) were improved 18 months after surgery.[19] The LAFA-study showed no statistically significant differences on any of the scales evaluated between laparoscopic and open surgery at any time point.[25]

For rectal cancer, 3 trials evaluated quality of life following laparoscopic and open surgery. The COREAN trial showed that sleep ($p = 0.004$), physical condition ($p = 0.007$) and fatigue ($p = 0.021$) were better 3 months after laparoscopy than open surgery. A greater frequency of sexual problems after surgery than before the intervention was

Table 6. Length of hospital stay following open and laparoscopic surgeries

Trial	Measure	Length of hospital stay, d		p value
		Open surgery	Laparoscopic surgery	
Colon cancer				
COLOR[14]	mean ± SD	9.3 ± 7.3	8.2 ± 6.6	< 0.001
COST[16]	median (IQR)	6 (5–7)	5 (4–6)	< 0.001
Barcelona[22]	mean ± SD	7.9 ± 9.3	5.2 ± 2.1	0.005
Liang et al.[23]	mean ± SD	14.0 ± 2.0	9.0 ± 1.0	< 0.001
LAPKON II[26]	mean ± SD median (range)	13.0 ± 8.6 12 (4–109)	13.4 ± 12.0 10 (1–123)	0.032
ALCCaS[27]	median (range) mean ± SD	8 (4–59) 10.6 ± 7.2	7 (1–55) 9.5 ± 7.4	< 0.001 0.07
CLASICC[21]	median (IQR)	9 (8–13)	9 (7–12)	NA
Rectal cancer				
CLASICC[21]	median (IQR)	11 (9–15)	13 (9–18)	NA
COREAN[34]	median (IQR)	9 (8–12)	8 (7–12)	0.06
Lujan et al.[36]	mean ± SD	9.9 ± 6.8	8.2 ± 7.3	0.11
Ng et al.[37]	median (range)	11.5 (3–38)	10.8 (5–27)	0.55
Ng et al.[39]	median (range)	10 (3–39)	8.4 (2–32)	0.013
Braga et al.[41]	mean ± SD	13.0 ± 10.0	10.0 ± 4.9	0.004
Zhou et al.[42]	mean ± SD	13.3 ± 3.4	8.1 ± 3.1	0.001

ALCCaS = Australasian Laparoscopic Colon Cancer Study; CLASICC = Conventional Versus Laparoscopic-Assisted Surgery in Patients with Colorectal Cancer; COLOR = Colon cancer Laparoscopic or Open Resection; COREAN = Comparison of Open versus laparoscopic surgery for mid and low Rectal cancer After Neoadjuvant chemoradiotherapy; COST = Clinical Outcomes of Surgical Therapy; IQR = interquartile range; NA = not available; SD = standard deviation.

observed for both groups ($p < 0.001$), with no difference between groups ($p = 0.29$). More miction problems were observed after laparoscopy than open surgery ($p < 0.001$).[34] Braga and colleagues[41] showed better general health status ($p < 0.001$), physical condition ($p < 0.001$) and social function ($p = 0.003$) with laparoscopy than open surgery, but only in the first year after the operation.[41] In the CLASICC trial, it was shown that men treated with laparoscopy tended to have worse global sexual ($p = 0.06$) and erectile function ($p = 0.07$); however, this difference was not significant. Conversion and total mesorectal excision were identified as prognostic factors negatively affecting sexual function. Although a decrease in global sexual function was generally observed in women following surgery, no difference was noted between groups. Urinary function was also similar following laparoscopic and open surgery in both men and women.[35]

Discussion

Oncologic outcomes

The first case series comparing laparoscopic and open surgeries for colon cancer treatment reported high recurrence rates at wound and port sites, raising doubts as to the oncologic efficacy of laparoscopy. Large randomized trials that followed were therefore attentive to oncologic outcomes, such as positive resection margins, number of lymph nodes harvested and recurrence rates at port sites. None of the trials included in this review showed any difference between open and laparoscopic procedures regarding these outcomes. Only in the COLOR trial were there more recurrences in the abdominal wall observed following laparoscopy than open surgery for colon cancer (5 at the port site and 2 at the tumour extraction site), but the difference was not significant ($p = 0.09$).[10] Three trials presented data on recurrence at trocar and scar sites following surgery for rectal cancer and reported only 1 recurrence (in the open surgery group).[33,37,39] Thus, it appears that initial concerns were not justified.

All but 1 trial studying colon cancer concluded that laparoscopy is noninferior to open surgery in terms of overall survival, disease-free survival and recurrence rate. The COLOR study group had set the noninferiority threshold at 7%, and the upper limit of the 95% CI for the 3-year disease-free survival difference just exceeded this, at 7.2%.[10] Though they could not totally exclude the possibility of inferiority, the authors still concluded that laparoscopy could be performed safely for the treatment of colon cancer. Moreover, when data are analyzed according to treatment received, as recommended in the CONSORT statement,[48] the noninferiority of laparoscopy is statistically confirmed.[10] On the other hand, only 1 trial concluded that laparoscopy was superior to open surgery for colon cancer treatment.[22] However, a number of biases were identified in that trial. First, trial design was based on the hypothesis that noninferiority would be declared if cancer-related survival after laparoscopy was less than 15% inferior to that after open surgery, which is a clinically unacceptable threshold according to the oncologic experts consulted. Second, equivalence of the 2 groups must be questioned, since the group assigned to laparoscopy received more postoperative chemotherapy than the group assigned to open surgery (61% v. 55%). It therefore seems inappropriate to conclude, based on the results of this single trial, that long-term outcomes of patients with colon cancer after laparoscopic resection are superior to those after open surgery.

The combined results of the 5 randomized trials included in this review confirm that laparoscopy is noninferior to open surgery for colon cancer treatment with respect to overall survival, disease-free survival and disease recurrence.[10,11,16,22,24] Results presented in 3 meta-analyses also strongly support these conclusions.[30–32]

Trials evaluating the laparoscopic procedure for rectal cancer had generally lower power than those evaluating laparoscopic colon cancer resection, thus explaining why trials accruing fewer than 200 patients were included in this review. Consequently, 6 randomized trials presenting data on survival and recurrence were retrieved and showed noninferiority of laparoscopic compared with open resection for rectal cancer in terms of overall and disease-free survival.[20,33,36,37,39,41] The equivalence of these 2 procedures is supported by 3 meta-analyses,[43–45] and was confirmed for both anterior and abdominoperineal resections.[20]

All trials retrieved included resections of the left, right or sigmoid colon for adult patients with stage I, II or III colon cancer or anterior or abdominoperineal resection of rectal cancer of any stage. A laparoscopic procedure is thus appropriate for these populations. In contrast, patients presenting with 1 or more of the following conditions were generally excluded: transverse colon cancer; morbid obesity; adjacent organ invasion; metastatic disease; cardiovascular, pulmonary or hepatic disease; inflammatory bowel disease; or need for emergency surgery. These conditions can be considered potential contraindications for laparoscopy, depending on the surgeon's experience. Notably, transverse colon resection poses many challenges, such as resection of the colic vessels and mobilization of the 2 colic segments before anastomosis. For these reasons, laparoscopic transverse colon resection should only be performed by surgical teams with extensive experience in laparoscopic colon resections. On the other hand, while patients with metastatic disease have generally been excluded from trials to avoid survival bias, clinical experience shows that laparoscopy can successfully be performed in some symptomatic patients presenting with obstruction or bleeding.

Short-term outcomes

Selected trials showed some short-term benefits of laparoscopy compared with open colorectal cancer

resection. These benefits include reduced need for analgesics, less postoperative pain, faster recovery of intestinal function and shorter hospital stay. While these differences were reported to be statistically significant, they represent only modest clinical benefits. However, 1 trial showed that partial and complete return to regular activities of daily life and return to work occurred twice as quickly after laparoscopy than open surgery.[24] This aspect could be a decisive factor in favour of laparoscopy for some patients.

Minor benefits regarding quality of life were also reported for patients who underwent laparoscopic surgery.[15,18,19,34,41] However, the validity of these results is open to question, since bias could not be excluded because patients were not blinded to treatment allocation and because no validated instrument specific to laparoscopic surgery is available. The questionnaires used in these trials addressed general health or cancer-related outcomes, which may have been less appropriate for quality of life assessment for patients undergoing surgery. Specifically for rectal cancer, it was shown that both urinary and sexual functions were not worse 3 months after laparoscopy compared with open surgery. Only in the COREAN trial were more problems with micturition after laparoscopy observed ($p = 0.002$);[34] however, this result was not replicated in a meta-analysis.[44]

Laparoscopy requires longer operative time than open surgery. Mean operative times for colon cancer resection varied between 95 and 184 minutes for open surgery and between 142 and 224 minutes for laparoscopy. The difference in duration for the 2 procedures thus ranges between 24 and 55 minutes. For rectal cancer, mean or median operative times ranged between 106 and 209 minutes with open surgery and between 120 and 262 minutes with laparoscopy, corresponding to a difference of 14–59 minutes between the 2 procedures. In the COLOR trial, differences between operative times tended to be smaller in centres with high volumes, suggesting that this disadvantage of laparoscopy is attenuated as the surgeon acquires more experience.[14] This trend was also observed for rectal cancer surgery.[49–51]

No clear conclusion can be drawn regarding complication rates following open or laparoscopic procedures for colon cancer, since 1 trial observed more complications following open surgery,[23] another showed more complications following laparoscopy,[27] and other trials observed similar complication rates for the 2 procedures.[14,16,21,24–26] In most trials, however, complication rates remained at an acceptable level following both procedures and were generally low grade (I and II).[16] In rectal cancer trials, intraoperative and postoperative complication rates ranged from 14% to 24% and from 6% to 52%, respectively, and were not statistically different between laparoscopic and open surgery. It is also presumed that the complication rate would be affected by the surgeon's experience, the complexity of the surgery performed and the patient selection criteria.

Few patients died as a result of colorectal cancer resection, regardless of the operative technique.

Conversion rate

In the trials included in this review, conversion rates ranged from 3% to 25% for colon cancer and from 0% to 33% for rectal cancer. Conversion was not uniformly defined across trials, making comparison difficult. Reasons for colon cancer conversion included advanced disease, large tumour size, inability to localize the tumour, inability to mobilize the colon, extensive adhesions, obesity and intraoperative complications, whereas reasons for rectal cancer conversion included substantial bleeding, difficulty in performing a safe resection, anastomotic leakage, rectal perforation, damaged ureter, obesity, advanced disease and narrowness of the pelvic cavity. Moreover, body mass index was identified as a significant factor for conversion in the context of rectal cancer resection ($p = 0.026$).[52] The lowest conversion rates were generally observed in trials where a single surgeon or team performed all laparoscopic surgeries,[23,24,33,34,36,40,41] suggesting that conversion rate is inversely correlated with surgeon experience. Furthermore, in the CLASICC trial, the conversion rate to open surgery for colorectal cancer decreased as more experience was gained: 38% in the first year of accrual to 16% in the sixth year.[21]

Conversion to open surgery is believed to have a negative impact on survival and morbidity outcomes. A subgroup analysis performed by the authors of the COST study showed that patients who underwent conversion experienced more complications than those whose colon surgery had been completed laparoscopically (7.8% v. 2.9%). Five-year overall survival was also lower in these patients (69% v. 80%).[17] In the CLASICC trial, converted surgery was associated with a hospital stay of up to 2 weeks longer than laparoscopy and with a higher complication rate (93% v. 50% following open surgery and 59% following laparoscopy).[21] On intention-to-treat analysis, patients who were converted intraoperatively to open surgery were appropriately included in the laparoscopic group. Conversion is a reality of normal practice and thus has to be considered in the evaluation of the safety of laparoscopy. Nevertheless, surgeries most susceptible to being converted should be identified preoperatively whenever possible so that these patients can be treated with open surgery to reduce the likelihood of complications.

Minimum training requirements

No randomized clinical trial has evaluated the minimum training requirements for safely performing laparoscopy for colon cancer treatment, despite the need to better inform surgeons in this regard. Most practice guidelines and consensus statements agree that surgeons need to

acquire a certain level of training.[53–56] In 2 trials, surgeons were required to have performed at least 20 laparoscopic colectomies in order to be recruited.[10,16] A few trials have tried to define the learning curve of laparoscopic colon resection, but these are primarily case series constituting a low level of evidence.[57–60] Despite the absence of evidence, it is reasonable to assume that the skills acquired from performing simple laparoscopic procedures are transferable to more complex surgeries.[59] In this sense, surgeons should first acquire experience through simple laparoscopic resections of benign lesions and then progressively integrate more complex procedures into their practices, including those involving cancer.

One prospective[61] and 3 retrospective[49–51] trials evaluated the impact of surgeon experience on oncologic outcomes following rectal cancer resection. Three of them showed that operative duration decreased significantly with the number of interventions performed.[49–51] Park and colleagues[51] observed a plateau after 90 interventions followed by a decrease in operative duration, whereas Ito and colleagues[50] reported that operative duration decreased from 228 to 179 minutes after more than 40 interventions had been performed. All 4 trials also showed a significant decrease in postoperative morbidity as the surgeon gained more experience (after 30–60 interventions had been performed, depending on the trial). Since inclusion criteria for patients and for surgeons were not the same for all trials, a general conclusion regarding the minimum number of cases to be performed to gain sufficient experience cannot be drawn. Nonetheless, the available evidence undoubtedly shows that surgeon experience and competence in laparoscopy for rectal cancer have a major impact on outcome.

Conclusion

Analysis of the scientific literature confirmed that for the curative treatment of colon and rectal cancer, laparoscopy is not inferior to open surgery with respect to overall survival, disease-free survival and rate of recurrence. In addition, laparoscopic surgery provides short-term advantages over open surgery, particularly a shorter hospital stay, reduced need for analgesics, faster recovery of intestinal function, and an earlier return to activities of daily life. In contrast, laparoscopic surgery requires a longer operative time.

Considering the evidence currently available, the CEPO recommends that laparoscopic resection be considered an option for the curative treatment of colon and rectal cancer (grade A recommendation); that decisions regarding surgical approach (laparoscopic or open surgery) for the curative treatment of colon cancer take into consideration the surgeon's experience, tumour stage, potential contraindications and patient expectations (grade D recommendation); and that laparoscopic resection for rectal cancer be performed only by appropriately trained surgeons who perform a sufficient volume annually to maintain competence (grade D recommendation).

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