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Oncology

Short-term outcomes after laparoscopic cytoreductive surgery in patients with limited peritoneal metastases from colorectal cancer ☆

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ABSTRACT

Background: The purpose of this study was to investigate the safety of laparoscopic cytoreductive surgery versus open surgery for patients with limited peritoneal metastases from colorectal cancer.

Methods: Laparoscopic surgery for patients with colorectal cancer with peritoneal metastases has been performed at our institution since December 2004. We retrospectively evaluated data from patients with colorectal cancer metastatic to the peritoneum, with a peritoneal cancer index ≤10. We compared short-term operative and survival outcomes in the laparoscopic cytoreductive surgery group and open cytoreductive surgery group.

Results: A total of 21 patients underwent open cytoreductive surgery and 42 underwent laparoscopic cytoreductive surgery, of whom 6 (14%) required open conversion. Clinicopathologic characteristics and operative outcomes were comparable between the groups. Complete cytoreduction was achieved in all patients in the laparoscopic cytoreductive surgery group and in 19 patients (91%) in the open cytoreductive surgery group ($P = .042$). Both the mean hospital stay and use of postoperative narcotics were significantly less in the laparoscopic cytoreductive surgery group than in the open cytoreductive surgery group. The type of operation (open cytoreductive surgery versus laparoscopic cytoreductive surgery) was not related to survival outcomes.

Conclusion: With careful selection by experienced laparoscopic surgeons, laparoscopic cytoreductive surgery was technically feasible and safe to treat colorectal cancer patients with limited peritoneal metastases.

Peritoneal carcinomatosis is a common form of colorectal cancer dissemination and has the worst prognosis among colorectal cancer metastases. Although there is lack of evidence from randomized controlled trials, studies have addressed the long-term survival benefits of combined cytoreductive surgery and intraperitoneal chemotherapy over systemic chemotherapy alone for colorectal peritoneal carcinomatosis.[1–3] In the 2017 update of the National Comprehensive Cancer Network guidelines, complete cytoreductive surgery or intraperitoneal chemotherapy is considered a treatment option for selected patients with limited peritoneal metastases for whom an R0 resection of the primary lesion can be achieved.[4] Peritoneal dissemination occurs when free intraperitoneal cancer cells are exfoliated from a primary tumor implant onto the visceral and parietal peritoneum.[5] For the maximum effect of both cytoreductive surgery and intraperitoneal chemotherapy, complete removal of all visible nodules should be achieved.[6] Complete cytoreductive surgery usually demands various combinations of peritonectomy and resection of intra-abdominal organs. Therefore, an extended laparotomy incision is usually recommended for these procedures.[7,8]

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In the operative resection of localized colorectal cancer, laparoscopic surgery decreases not only the total length of the abdominal incision(s), but also pain, recovery time, wound-related complications, and overall morbidity compared with open surgery. Moreover, postoperative immunologic function is believed to be better preserved after laparoscopic surgery than after open surgery.[9,10] Randomized controlled trials assessing long-term oncologic safety have established laparoscopic surgery as the standard approach to localized colorectal cancer.[11,12] Laparoscopic surgery is now commonly used to assess the extent of peritoneal dissemination and resectability and to administer palliative intraperitoneal chemotherapy for patients with peritoneal carcinomatosis, but some concerns remain regarding the technical difficulty and the oncologic safety of a laparoscopic approach for a radical, complete, cytoreductive resection of peritoneal metastases.[13–15]

The safety and feasibility of laparoscopic cytoreductive surgery have only been explored in a limited number of studies.[16,17] To date, only three retrospective studies have compared laparoscopic and open cytoreductive surgery.[18–20] Two of these included small numbers of patients with heterogeneous characteristics and noncolorectal cancers.[18,20] Although we performed one of these three studies, our study was also small and included some patients undergoing palliative intraperitoneal chemotherapy.[19] In the present study, we hypothesized that a laparoscopic approach offers a quicker postoperative recovery than open surgery, with comparable oncologic outcomes in selected patients with limited colorectal peritoneal carcinomatosis. Therefore, the purpose of this study was to determine the completeness of cytoreduction, postoperative outcomes, and survival outcomes of laparoscopic versus open cytoreductive surgery for patients with limited peritoneal carcinomatosis, which we defined as a peritoneal cancer index (PCI) score of 10 or less.

Methods

Patients

At our institution, laparoscopic surgery has been performed for colorectal cancer patients with peritoneal metastases since December 2004. Data from an institutional database of a consecutive series of patients who had undergone cytoreductive surgery and intraperitoneal chemotherapy for peritoneal metastases from colorectal cancer between November 2004 and December 2017 were reviewed retrospectively. Exclusion criteria were peritoneal metastases with a PCI score >10, nonresected extraperitoneal metastases, and treatment with palliative intention. The patients had been provided information regarding diagnostic laparoscopy, cytoreductive surgery, and intraperitoneal chemotherapy. The choice between laparoscopic cytoreductive surgery (LCRS) and open cytoreductive surgery (OCRS) was mainly made during diagnostic laparoscopy. All patients had provided written informed consent before the operation. Institutional review board approval was obtained for this retrospective study.

Details of laparoscopic procedures

Laparoscopic operations were performed by 4 experienced laparoscopic surgeons. One 11-mm optical port was placed to introduce a 0- or 30-degree laparoscope in the periumbilical area in a region where there was no evidence of metastatic nodules. Three or four 5-mm working ports were placed in the abdominal quadrants. Step-by-step exploration from the peritoneal reflection to the subphrenic and subhepatic area was performed laparoscopically. The choice of operation type was based on disease characteristics (mass sizes, PCI score, location, and infiltration), the general condition of the patient's abdominal cavity (eg, severe adhesions from previous surgery), and technical feasibility. The goal of operative intervention was to remove all visible nodules in accordance with Sugarbaker's recommendations.[7] The greater omentum was removed in all patients, regardless of the presence of metastatic nodules. Organ resection, such as colectomy, oophorectomy, splenectomy, or hysterectomy, was performed to achieve complete removal of visceral peritoneal metastases. Parietal peritonectomy was performed in areas where visible nodules were found. A mini laparotomy was used to retrieve specimens and to treat the small-bowel mesentery. Port incisions and mini laparotomy were used to introduce catheters for hyperthermic intraperitoneal chemotherapy (HIPEC) or early postoperative intraperitoneal chemotherapy (EPIC). The extent of peritoneal carcinomatosis was categorized according to the PCI score.[21] The completeness of cytoreduction (CCR) was assessed at the end of the operation and classified into four categories: CCR-0 (no visible residual nodules), CCR-1 (residual nodules $\leq$2.5 mm in diameter), CCR-2 (residual nodules between 2.5 mm and 2.5 cm in diameter), and CCR-3 (residual nodules $>$2.5 cm in diameter).[21]

Intraperitoneal chemotherapy and postoperative management

Patients received either EPIC or HIPEC after cytoreductive surgery. The protocol for EPIC was mitomycin C (10mg/m^2/day) on day 1 and 5-fluorouracil (700mg/m^2/day) on days 2 to 5 intraperitoneally during the early postoperative period as described in our earlier study.[19] We started HIPEC on December 2014 after our institution introduced the use of a Hyperthermia Pump (Belmont Instrument Corp, Billerica, MA, USA). The protocol for HIPEC was perfusion with mitomycin C (35 mg/m^2) for 90 min, with an inflow temperature of 41°C to 43°C. We did not use an enhanced recovery protocol for perioperative management. Intravenous, patient-controlled analgesia was used as needed with intravenous tramadol administered as rescue analgesia. Clear liquids orally were started on postoperative day 6 after EPIC or on postoperative day 3 after HIPEC. A solid diet was allowed the next day if tolerated.

Follow-up evaluation

We recommended that all patients undergo adjuvant systemic chemotherapy and follow up for 5 years or more. Follow-up evaluation consisted of a physical examination and the measurement of serum tumor markers every 3 months, with abdominal computed tomography every 6 months.

Statistical analysis

Outcomes of interest included the CCR score, postoperative recovery, grade 3 to 5 morbidity according to the National Cancer Institute Common Terminology Criteria for Adverse (https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5 × 7.pdf), and 3-year disease-free and overall survival. Statistical analyses were performed to compare outcomes between the LCRS and OCRS groups. Quantitative data were summarized as means with standard deviations. Categorical variables were described as numbers (percentages). Statistically significant differences were evaluated with the Mann–Whitney test, Student t test, χ^2 test, and Fisher exact test, as appropriate. Survival rates were estimated by Kaplan–Meier analysis and compared with the log-rank test. A Cox proportional hazards regression model with forward selection of variables based on univariate analyses was used to estimate the degree to which variables affected survival. All tests were 2-sided comparisons, with statistical significance defined as $P < .05$. All calculations were performed with SPSS software version 21 (SPSS, Chicago, IL, USA).

Table 1
Cause of open surgery.

	No. of patients
Decision during laparoscopic exploration, n (%)	N = 21
Large primary tumor	9 (42.9)
Large ovarian mass	6 (28.6)
Adhesions from primary tumor operation	4 (19.0)
Difficult location (subphrenic, cardiophrenic angle)	2 (9.5)
Decision during laparoscopic surgery (Open conversion), n (%)	N = 6
Difficult location (subhepatic, ureter)	3 (50.0)
Firmly fixed primary tumor	3 (33.3)
Adhesions from primary tumor operation	1 (16.7)
Newly identified peritoneal nodule during open exploration	0 of 27 patients

Results

Patient characteristics

A total of 71 patients had peritoneal metastases of colorectal cancer with PCI scores of 10 or less, 8 of whom had unresectable extraperitoneal metastases and were therefore excluded from the analysis. There were 42 patients in the LCRS group and 21 in the OCRS group. Of the patients in the LCRS group, 6 (14%) required open conversion because the surgeon was concerned that there was a risk of CCR-1 or more with the laparoscopic approach. The reasons for deciding to perform OCRS or open conversion during LCRS are presented in Table 1. The main reasons for OCRS were either large primary tumors or ovarian masses in women and because of open conversion owing to challenging locations of peritoneal metastases, such as in the subphrenic parietal peritoneum or adjacent to the ureter. Among patients who underwent OCRS or open conversion, there were no cases having additional nodules newly found during open surgery, and no patients required a change in the operative plan decided at laparoscopy. Relevant patient characteristics were similar in the 2 groups, except for a significant difference in sex distribution (38% were women in the LCRS vs 71% in the OCRS group; $P = .013$; Table 2).

Treatment details and operative outcomes

CCR-0 was achieved in all patients (100%) in the LCRS group and in 19 of the 21 patients (91%) in the OCRS group ($P = .042$). When the abdominopelvic area was divided into 10 regions (central, epigastric, right upper, right lower, right flank, left upper, left lower, left flank, pelvis, and small-bowel mesentery) for peritoneal dissection, the mean number of treated regions did not differ between the 2 groups. Operative time, intraoperative blood loss, time to passing flatus, incidence of postoperative operative morbidity (ie, wound infection, leakage, and ileus), and incidence of systemic toxicity (ie, neutropenia) were similar between the 2 groups (Table 3). Reoperation for anastomotic leakage was performed on 1 patient in the LCRS group and radiologic intervention for acalculous cholecystitis was necessary for another in the same group. The patient-controlled analgesia and rescue narcotics were used significantly less frequently in the LCRS than in the OCRS group. The mean postoperative hospital stay was less in the LCRS than the OCRS group (14.3 ± 7.3 vs 20.2 ± 12.2 days; $P = .019$). Postoperative 90-day mortality occurred in 1 patient in each group.

Survival analyses

The median duration of follow-up was 33.4 months for the LCRS and 19.7 months for the OCRS group ($P = .407$). The 3-year overall survival rate was 67% in the LCRS group and 66% in the OCRS group (Fig 1, *A*). The median overall survival period for patients in the LCRS group was 57 months, which was comparable with that of patients in the OCRS group (38 months; $P = .336$). The disease-free survival curves and peritoneal recurrence-free survival curves were similar between the LCRS and OCRS groups (3-year disease-free survival: 39% vs 33%, respectively, $P = .175$; 3-year peritoneal recurrence-free survival: 51% vs 53%, respectively, $P = .993$; Fig 1, *B* and *C*). The survival curves of the LCRS and OCRS groups were also comparable when patients with a PCI 1 to 5 and a PCI of 6 to 10 were grouped and analyzed separately (Fig 2). The locations of all initial recurrences are presented in Table 4. Patients in the LCRS group tended to have peritoneum as the first recurrence site more frequently than patients in the OCRS group, and this tendency decreased when patients with a history of other metastases were excluded.

Univariate analysis revealed that a PCI score >5, CCR-1, occurrence of systemic toxicity, and concurrent distant metastasis were risk factors for a lesser overall survival (Table 5). The type of operation (open versus laparoscopic) was not associated with cancer-specific survival according to univariate or multivariate analysis. According to multivariate analysis, a CCR-1 (HR = 8.928, $P = .014$) and systemic toxicity (HR = 8.928, $P = .003$) were independently associated with overall survival.

Table 2
Characteristics of patients.

Variables*	OCRS (n = 21)	LCRS (n = 42)	*P*
Age (years)	51.2 (11.4)	55.7 (13.7)	0.206
Body mass index (kg/m^2)	22.3 ± 3.9	23.7 ± 3.2	0.138
Sex			0.013
Male	6 (28.6)	26 (61.9)	
Female	15 (71.4)	16 (38.1)	
ASA class			0.423
1	9 (42.9)	12 (28.6)	
2	11 (52.4)	29 (69.0)	
3	1 (4.8)	1 (2.4)	
Previous abdominal surgery	2 (9.5)	8 (19.0)	0.329
Neoadjuvant chemotherapy	2 (9.5)	1 (2.4)	0.209
Location of primary tumor			0.127
Colon	16 (76.2)	38 (90.5)	
Rectum	5 (23.8)	4 (9.5)	
Serum tumor marker			
CEA-elevation	6 (28.5)	14 (33.3)	
CA19-9-elevation	10 (47.6)	11 (26.2)	
Time of peritoneal metastasis			0.180
Synchronous	12 (57.1)	31 (72.1)	
Metachronous	9 (42.9)	11 (26.2)	
Other distant metastasis			0.117
No	14 (66.7)	37 (88.1)	
Concurrently resected	5 (23.8)	4 (9.5)	
Previously resected	2 (9.5)	1 (2.4)	
Pathologic T classification			0.105
T3	12 (57.1)	15 (35.7)	
T4	9 (42.9)	30 (64.3)	
Pathologic N classification			0.117
N0	4 (19.0)	7 (16.7)	
N1	5 (23.8)	21 (50.0)	
N2	12 (57.1)	14 (33.3)	
Histologic differentiation			0.486
Well, moderate	16 (76.2)	35 (83.3)	
Poor, mucinous, signet ring cell	5 (23.8)	7 (16.7)	
Neoadjuvant chemotherapy	2 (9.5)	1 (2.4)	0.209
Adjuvant chemotherapy	18 (85.7)	38 (90.5)	0.571

ASA, American Society of Anesthesiology; CEA, carcino-embryonic antigen; CA, carbohydrate antigen.
* Mean ± SD or n (%).

Discussion

In this study, we found that, with appropriate patient selection based on exploratory laparoscopy findings, laparoscopic surgery

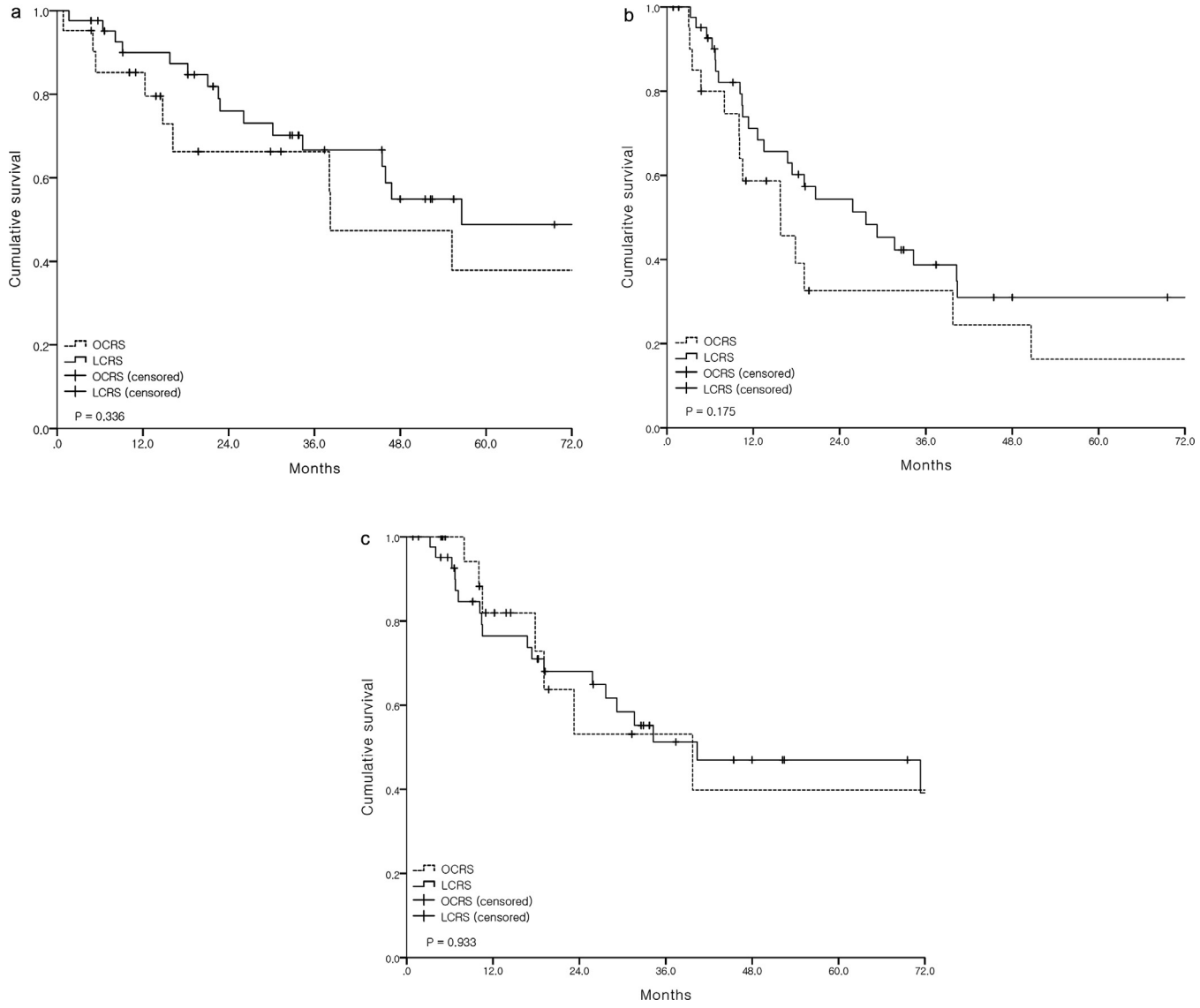

Fig. 1. Kaplan–Meier survival curves. (*A*) Cancer-specific survival. (*B*) Disease-free survival. (*C*) Peritoneal recurrence-free survival.

can be an effective option for curative treatment of colorectal cancer with peritoneal metastases of limited extent. Unnecessary laparotomy was avoided in 36 (57%) of our study cohort. There was no difference in short-term outcomes between the LCRS and OCRS groups. Earlier reports of LCRS have been primarily preliminary experience and have included small numbers of patients with less aggressive peritoneal malignancies, such as pseudomyxoma peritonei, multicystic mesothelioma, or appendiceal disease.[16,18] One of the strengths of our current study is that all patients had peritoneal metastases from colorectal cancer, which has a more aggressive biology than other peritoneal malignancies.[21]

The overall morbidity rate after LCRS was comparable with that after OCRS. The incidence of operative complications in this study was similar to previously reported rates.[16,18] The well-known advantages of laparoscopic colorectal cancer surgery over open surgery are the use of a shorter total incision length, less pain, fewer wound-related complications, decreased blood loss, earlier recovery, and a lesser hospital stay.[22,23] Although we did not evaluate postoperative pain scores, we found that patient-controlled analgesia and rescue narcotics were used less frequently in the LCRS group. The finding that the mean hospital stay in the LCRS group was 6 days less than that in the OCRS group is also consistent with the known advantages of laparoscopic surgery. We identified no LCRS-related intraoperative complications. We found that 6 of 42 patients required conversion to an open approach after the initial laparoscopic exploration to achieve CCR-0, but not in response to intraoperative complications. The clinical outcomes of these patients did not differ from those of the other patients.

Laparoscopic exploration has generally been used to diagnose peritoneal metastases and to identify candidates for complete OCRS and intraperitoneal chemotherapy. It is useful for avoiding an unnecessary laparotomy in patients with massive peritoneal metastases.[14,24] Passot et al[24] reported that diagnostic laparoscopy enabled identification of 82% of peritoneal recurrences in patients at high risk of peritoneal recurrence from colorectal cancer but who did not have preoperative evidence of such metastases. When laparoscopic exploration was feasible, the sensitivity and specificity for diagnosing peritoneal metastases was greater than 90%. In that study, however, satisfactory laparoscopic evaluation was feasible in only about half of the patients, and laparoscopy tended to underestimate the PCI in comparison with open evaluation. That prospective trial included only patients at risk of metachronous peritoneal recurrence in whom adhesions from previous surgery could hinder accurate evaluation of the PCI throughout the peritoneum. Al-

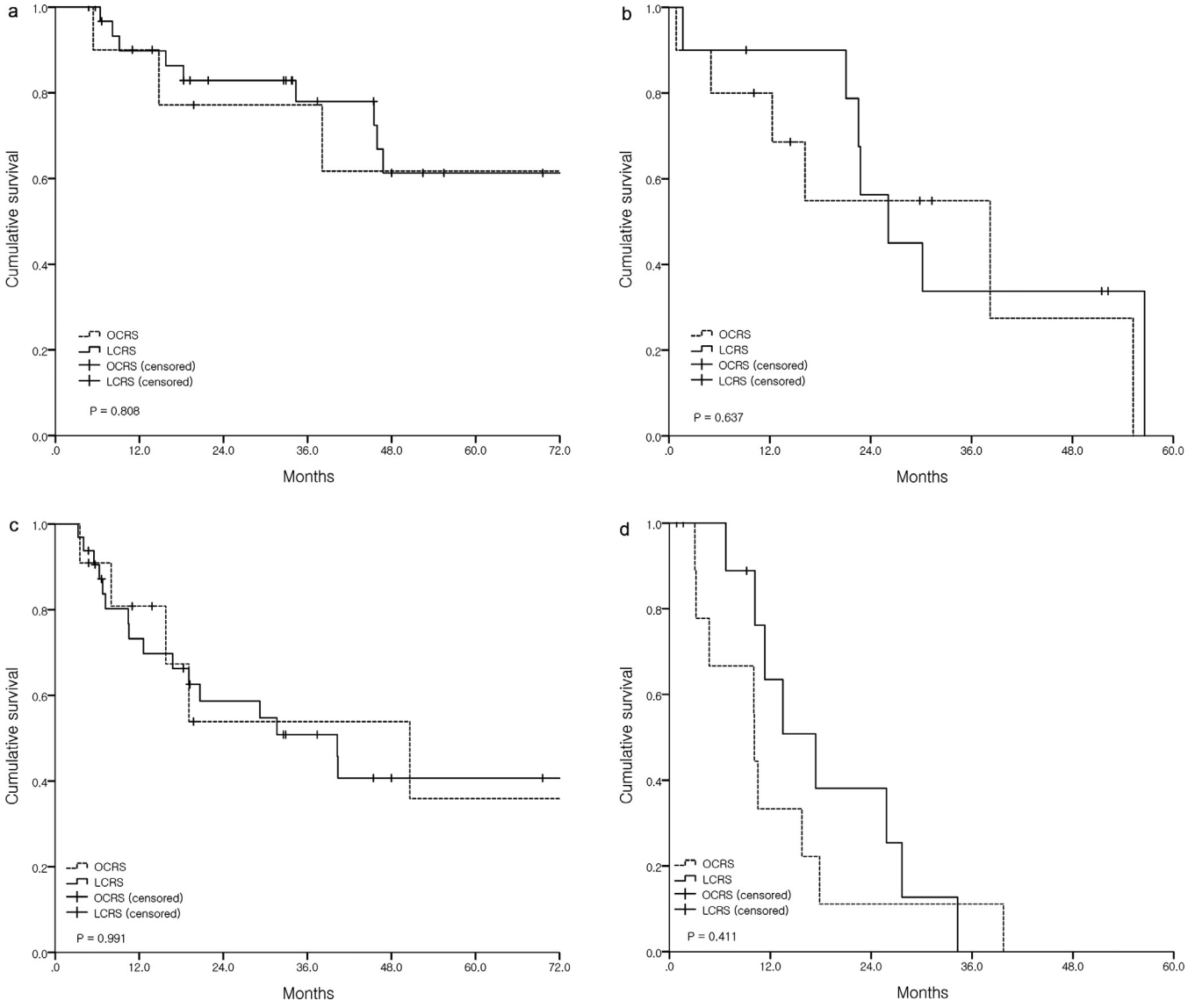

Fig. 2. Kaplan–Meier survival curves. (*A*) Cancer-specific survival in patients with PCI ≤5. (*B*) Disease-free survival in patients with PCI ≤5. (*C*) Cancer-specific survival in patients with PCI 5 to 10. (*D*) Disease-free survival in patients with PCI 5 to 10.

though postoperative adhesions are associated with the type of earlier operation and surgical procedure,[25] the authors provided no information regarding the initial operative type (open or laparoscopic) for colorectal cancer. Moreover, in multicenter studies, there is underlying heterogeneity in the techniques of individual surgeon. In our study, among the 27 patients who ultimately underwent open surgery, none had additional nodules found during open exploration. This finding is likely attributed to the fact that more than 60% of our patients had synchronous peritoneal metastases and that patients with PCI >10 were excluded.

The recent PRODIGE 7 clinical trial[26] demonstrated the importance of curative resection of colorectal peritoneal metastases by identifying excellent survival outcomes after cytoreductive surgery with or without HIPEC. The median overall survival of all patients in the current study was 55 months, which is consistent with the results of the PRODIGE 7 trial.[26] Both LCRS and OCRS achieved similar short-term oncologic outcomes in terms of completeness of cytoreductive surgery and survivals. During open procedures, a self-retaining retraction system is used for exposure of all quadrants of the abdomen and for retraction of the abdominal wall for stripping parietal peritoneum. When performing laparoscopic procedures, pneumoperitoneum can provide traction of the abdominal wall, and a laparoscopic videoscope magnifies the surgical field of view, allowing visualization of small peritoneal nodules and facilitating complete cytoreduction.[7] Laparoscopic surgery demands specific operative techniques and involves a procedural learning curve. In the present study, all LCRS procedures were performed by 1 of 4 experienced laparoscopic surgeons, each with more than 5 years of experience in laparoscopic colorectal surgery and who perform >150 cases per year. Recent improvements in operative technologies and extensive experience with laparoscopic surgery at our center have enabled us to perform LCRS safely in appropriately selected patients. We recommend that LCRS be performed by a surgeon with extensive experience in both laparoscopic and cytoreductive surgery.

Open conversion was required in 6 of 42 patients (14%) because the surgeon believed there to be a risk of a CCR-1 or more if an LCRS was to be performed. The most common reason for open conversion was because of a difficult location for laparoscopic peritonectomy. Metastases to the subphrenic parietal peritoneum, subhepatic space, and porta hepatis are challenging to perform laparoscopically. In these areas, the liver can interfere with the view of

Table 3
Operation data and postoperative recovery.

Variables*	OCRS (n = 21)	LCRS (n = 42)	*P*
Operation time (skin to skin), min	269.8 ± 121.2	236.7. ± 87.2	0.218
Operation time (cytoreduction), min	229.8 ± 87.8	207.1 ± 62.9	0.273
Blood loss, ml	235 ± 350.3	98.9 ± 165.7	0.185
Peritoneal cancer index			0.056
1–5	11 (52.4)	32 (76.2)	
6–10	10 (47.6)	10 (23.8)	
Completeness of cytoreduction			0.042
CCR-0	19 (90.5)	42 (100.0)	
CCR-1	2 (9.5)	0 (0.0)	
Number of peritonectomy regions	2.1 ± 0.9	1.9 ± 1.1	0.296
Organ resection			
Colectomy	13 (61.9)	33 (78.6)	0.160
Gastrectomy	0 (0.0)	1 (2.4)	0.476
Small bowel resection	3 (14.3)	2 (4.8)	0.187
Hysterectomy	5 (23.8)	1 (2.4)	0.006
Oophorectomy	10 (47.6)	7 (16.7)	0.009
Splenectomy	0 (0.0)	1 (2.4)	0.476
Cholecystectomy	0 (0.0)	2 (4.8)	0.310
Hepatic resection	0 (0.0)	1 (2.4)	0.476
Intraoperative complication	0 (0.0)	0 (0.0)	
Type of intraperitoneal chemotherapy			0.554
EPIC	14 (66.7)	31 (73.8)	
HIPEC	7 (33.3)	11 (26.2)	
Surgical complications	3 (14.4)	4 (9.5)	0.571
Systemic toxicity	8 (38.1)	9 (21.4)	0.160
Grade 3–5 morbidity	7 (33.3)	7 (16.7)	0.134
Reoperation or intervention	0 (0.0)	2 (4.8)	0.310
90-day mortality	1 (4.8)	1 (2.4)	0.611
Time to flatus, days	5.5 ± 2.0	5.0 ± 1.8	0.447
Time to liquid diet, days	5.7 ± 2.0	5.0 ± 2.1	0.216
Hospital stay, days	20.2 ± 12.2	14.3 ± 7.3	0.019
Use of patient-controlled analgesia	19 (90.5)	26 (61.9)	0.018
Rescue narcotics, times	3.8 ± 4.3	1.3 ± 3.3	0.012
Postoperative chemotherapy	18 (85.7)	38 (90.5)	0.571

CCR, completeness of cytoreduction; EPIC, early postoperative intraperitoneal chemotherapy; HIPEC, hyperthermic intraperitoneal chemotherapy; IPC, intraperitoneal chemotherapy; CRS, cytoreductive surgery.
* Mean +/- SD or n (%).

Table 4
Location of initial recurrence.

Parameters*	OCRS	LCRS	P
All cases of recurrence	(n = 13)	(n = 24)	0.183
Peritoneum only	4 (30.8)	15 (62.5)	
Peritoneum and other metastasis	3 (23.1)	3 (12.5)	
Other distant metastasis only	6 (46.2)	6 (25.0)	
Cases with no concurrent other distant metastasis	(n = 8)	(n = 22)	0.198
Peritoneum only	2 (13.3)	13 (59.1)	
Peritoneum and other metastasis	3 (37.5)	3 (13.6)	
Other distant metastasis only	3 (37.5)	6 (27.3)	
Cases without any history of other distant metastasis	(n = 7)	(n = 21)	0.240
Peritoneum only	2 (28.6)	12 (57.1)	
Peritoneum and other metastasis	3 (42.6)	7 (33.3)	
Other distant metastasis only	2 (28.6)	6 (28.6)	

OCRS, open cytoreductive surgery; LCRS, laparoscopic cytoreductive surgery.
* n (%).

operative field. Moreover, important structures (left gastric artery, gastroduodenal artery, inferior vena cava, bile duct, duodenum, and pancreas) are located in these areas, making it difficult to dissect the peritoneum safely. In the present study, all patients with multiple metastatic nodules in these areas underwent open surgery. In other studies of LCRS, the upper abdomen, including these areas, was rarely involved.[16,18] The technical strategies for laparoscopic approaches for these complex areas requires further investigation in future studies.

Survival curves of both groups were comparable when compared for patients with PCI ≤5 and patients with PCI >5, separately. After controlling for confounding factors, the operative approach had no impact on overall or disease-free survival according to multivariate analysis. As in other studies,[27] the most common site of initial recurrence in all patients in both groups in the current study was peritoneal metastasis. Although the peritoneum was more frequently the first recurrence site in the LCRS than in the OCRS group, this difference decreased when patients with a history of other metastases were excluded. These findings suggest that LCRS does not impair the efficacy of cytoreductive surgery and intraperitoneal chemotherapy in controlling peritoneal disease.

Nevertheless, this retrospective study has several limitations that should be kept in mind when interpreting our results. First, we concede that selection bias could not be eliminated completely in this study. Patient characteristics in both groups were not balanced at the baseline because of our selection process for LCRS. Although most baseline characteristics did not differ between the groups, the OCRS group included a greater proportion of women and of metachronous peritoneal metastases, a history of other distant metastases, and a PCI >5 than did the LCRS group. Second, the retrospective nature of this study meant that individual details of disease, such as location, infiltration, and extent, might not be as-

Table 5
Univariate and multivariate analysis of factors affecting survival outcomes

Survival and variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P*	HR	95% CI	*P*
Cancer-specific survival						
PCI (6–10)	3.30	1.49–7.35	.003			
CCR (CCR-1)	6.80	1.46–31.63	.015	11.85	2.38–58.98	.003
Systemic toxicity (yes)	3.36	1.54–7.34	.002	3.95	1.76–8.90	.001
Concurrent distant metastasis (yes)	2.91	1.05–8.10	.041			
Type of operation (LCRS)	1.47	0.67–3.23	.338			
Disease-free survival						
PCI (6–10)	3.38	1.72–6.65	< .001			
CCR (CCR-1)	6.61	1.46–30.03	.014	13.09	2.69–63.63	.001
Systemic toxicity (yes)	4.63	2.21–9.69	< .001	5.42	2.52–11.64	< .001
Concurrent distant metastasis (yes)	2.90	1.26–6.67	.013			
Type of operation (LCRS)	0.64	0.33–1.23	.180			
Peritoneal-recurrence survival						
PCI (6–10)	2.08	0.92–4.71	.078			
CCR (CCR-1)	2.67	0.34–20.81	.347			
Systemic toxicity (yes)	3.41	1.40–8.29	.007	3.41	1.40–8.29	.007
Concurrent distant metastasis (yes)	1.99	0.68–5.84	.212			
Type of operation (LCRS)	1.04	0.43–2.49	.934			

HR, hazard ratio; CI, confidence interval

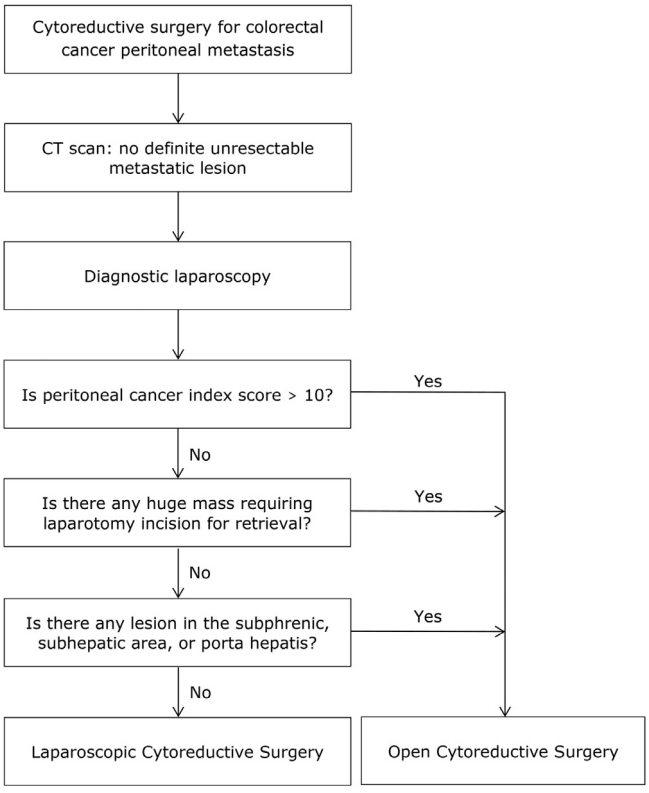

Fig. 3. Flowchart of the patient selection process for laparoscopic cytoreductive surgery.

sessed reliably. Third, this study was based on the long-term experience of a single center that specializes in minimally invasive colorectal cancer surgery. The small number of patients may limit the statistical analysis and generalizability of the findings. We stress that there were no significant changes in surgical practice at our institution during the study period.

In conclusion, our experience of LCRS with intraperitoneal chemotherapy for patients with limited peritoneal metastases from colorectal cancer (PCI <10) suggests that this treatment is technically safe and feasible in highly selected patients. Under the careful supervision of an experienced surgeon, LCRS did not impair the efficacy of cytoreductive surgery. According to currently available evidence, including this study, LCRS should be performed by surgeons with experience in both laparoscopic and cytoreductive surgery after applying the selection criteria of extent of peritoneal dissemination (PCI ≤ 10), laparoscopic accessibility of disease location (not subphrenic, subhepatic, or porta hepatis), and the condition of the abdomen (ie, minimal or no adhesions; Fig 3). The findings of this study provide a basis for future prospective evaluation. Prospective randomized trials to ascertain the value of laparoscopic surgery for patients with colorectal peritoneal metastases are warranted.

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