

Laparoscopic cytoreductive surgery and HIPEC for colorectal and appendiceal peritoneal metastases: a propensity score-matched comparative study

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Abstract

Background

Laparoscopic cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS–HIPEC) has emerged as a minimally invasive alternative for selected patients with colorectal and appendiceal peritoneal metastases (PM). However, evidence comparing laparoscopic and open CRS–HIPEC remains limited.

Methods

We conducted a retrospective cohort study including all consecutive patients with colorectal or appendiceal PM undergoing CRS–HIPEC at our institution. Propensity score matching (1:2) was performed using age, sex, ASA score, peritoneal cancer index (PCI), and primary tumor location. Perioperative outcomes were compared between laparoscopic and open approaches.

Results

Nineteen laparoscopic CRS–HIPEC procedures were matched to 38 open CRS–HIPEC controls from a prospectively maintained database (April 2019 to October 2025). Baseline demographics, burden of disease, and surgical complexity were comparable between groups. Median operative time (240 vs. 312 min, $p = 0.0045$) and intraoperative blood loss (100 vs. 300 mL, $p = 0.0188$) were lower in the laparoscopic group. Hospital stay was shorter in the laparoscopic cohort (4 vs. 8 days, $p = 0.0049$). Overall postoperative complications were lower following laparoscopic CRS–HIPEC (26.3% vs. 61.3%, RR 0.43, 95% CI 0.20–0.91, $p = 0.0215$), while major complication rates (Clavien–Dindo $\geq$ III) were similar (5.3% vs. 5.9%, $p = 1.0$). No difference was found in overall survival (94.7% vs. 78.9%, $p = 0.247$).

Conclusions

Laparoscopic CRS–HIPEC is safe and feasible in selected patients with low-PCI colorectal and appendiceal peritoneal metastases when performed by surgeons trained in advanced oncologic laparoscopic procedures. This approach is associated with faster postoperative recovery and reduced overall morbidity while maintaining comparable major complication rates and favourable short-term oncologic outcomes. Prospective multicenter studies are needed to confirm long-term oncologic results.

Introduction

Peritoneal metastases (PM) from colorectal cancer represent a distinct pattern of disease spread associated with significant morbidity and limited survival. Cytoreductive surgery (CRS) combined with

hyperthermic intraperitoneal chemotherapy (HIPEC) is an established treatment option for carefully selected patients with colorectal peritoneal metastases (CRPM) [2, 3, 7, 8, 13].

As surgical expertise and minimally invasive techniques have evolved, laparoscopic CRS–HIPEC has emerged as an alternative for patients with low-volume, favourably distributed disease. Proposed advantages include reduced surgical trauma, shorter postoperative recovery, and comparable oncologic outcomes [1, 14]. Adequate experience in advanced oncologic laparoscopic surgery is considered essential to achieve favourable perioperative results [6]. Despite these potential benefits, high-quality comparative evidence remains scarce, and most reported series involve heterogeneous tumour populations or lack matched comparisons [5].

We hypothesised that laparoscopic CRS–HIPEC in carefully selected patients with low-PCI colorectal and appendiceal PM would achieve comparable major morbidity to open CRS–HIPEC while offering improved perioperative outcomes. This study compares both approaches using propensity score matching to minimise selection bias, in a specialised colorectal cancer and peritoneal oncology unit at a tertiary referral hospital.

Methods

Study design and population

This was a retrospective observational cohort study including all consecutive patients who underwent laparoscopic CRS–HIPEC for PM of colorectal or appendiceal origin at our institution (LAP group). Data were extracted from a prospectively maintained REDCap database specifically designed for CRS–HIPEC procedures. No formal sample size calculation was performed, as the study included all consecutive laparoscopic CRS–HIPEC cases performed during the study period.

Collected variables included patient demographics (age, sex, body mass index [BMI]), American Society of Anesthesiologists (ASA) physical status, primary tumour location, Peritoneal Carcinomatosis Index (PCI), disease characteristics, intraoperative variables (type and extent of peritonectomy procedures, number of anastomoses, operative time, estimated blood loss, intraoperative temperature, and intraperitoneal chemotherapy [IPC] regimen), and postoperative outcomes (length of intensive care unit [ICU] and hospital stay, postoperative complications, need for reoperation, and mortality).

Propensity score matching

To minimise selection bias, a 1:2 nearest-neighbour propensity score matching without replacement was performed using R software (MatchIt package), matching each laparoscopic case to two open CRS–HIPEC controls (OPEN group). Matching covariates included age, sex, ASA physical status, intraoperative PCI, and primary tumour location.

Surgical technique

All patients selected for CRS–HIPEC underwent complete laparoscopic exploration with PCI evaluation before cytoreduction. HIPEC was delivered at 42°C according to institutional protocols: Cisplatin (CDDP) 75 mg/m² plus Mitomycin C 15 mg/m² for 60 minutes, Mitomycin C 35 mg/m² for 90 minutes, or Oxaliplatin 460 mg/m² for 30 minutes. Oxaliplatin-based HIPEC was subsequently abandoned in favour of Mitomycin C–based protocols following publication of the PRODIGE 7 trial results [4, 9].

Outcomes and statistical analysis

The primary outcome was postoperative morbidity, defined as the occurrence of any complication and major complications classified as Clavien–Dindo (CD) grade III or higher. Secondary outcomes included length of hospital and ICU stay, 30-day readmission rate, reoperation rate, postoperative mortality, disease-free status, and overall survival at last follow-up.

Statistical analyses were performed by the corresponding author. Continuous variables were summarised as median (interquartile range [IQR]) and compared using the Mann–Whitney U test. Categorical variables were expressed as counts (percentages) and compared using the χ^2 test or Fisher’s exact test as appropriate. Effect sizes for binary outcomes are reported as relative risk (RR) with 95% confidence intervals (CI). All tests were two-sided; statistical significance was set at $p < 0.05$. Analyses were performed using R software (version 4.3.0, R Foundation for Statistical Computing, Vienna, Austria).

Results

Patients operated between April 2019 and October 2025 were included. Of 183 patients who underwent CRS–HIPEC for PM of colorectal or appendiceal origin at our institution, 19 laparoscopic procedures were identified and matched to 38 open CRS–HIPEC controls, yielding a final cohort of 57 patients.

Baseline characteristics

Baseline demographic and oncologic characteristics were comparable between groups (Table 1). No significant differences were observed in age, sex, ASA score, BMI, synchronous disease rate, previous abdominal surgery, Prior Surgical Score (PSS), nodule size, PCI, or primary tumour location. Although PSS tended to be higher in the OPEN group (median 0 vs. 1, $p = 0.460$), this did not reach statistical significance.

Table 1
Baseline characteristics

Variable	LAP n = 19	OPEN n = 38	p value
Age (years, median)	65	69	0.334
Male sex (%)	57.9%	48.4%	0.576
ASA score III–IV (%)	10.5%	12.9%	1.000
BMI (kg/m ² , median)	27.8	27.1	0.822
Synchronous disease (%)	36.8%	22.6%	0.356
Previous cancer surgery (median)	1	1	1.000
Previous abdominal surgery (median)	2	2	1.000
PSS (median)	0	1	0.460
Nodule size	> 5 mm, < 5 cm	> 5 mm, < 5 cm	1.000
PCI (median)	2	3	0.460
Primary tumor — Appendix, n (%)	11 (57.9%)	16 (42.1%)	0.278
Primary tumor — Right colon, n (%)	3 (15.8%)	5 (13.2%)	1.000
Primary tumor — Left colon/sigmoid, n (%)	4 (21.1%)	15 (39.5%)	0.236
Primary tumor — Rectum, n (%)	1 (5.2%)	1 (2.6%)	1.000
Primary tumor — Transverse colon, n (%)	0 (0%)	1 (2.6%)	1.000
<i>ASA: American Society of Anesthesiologists; BMI: Body Mass Index; PSS: Prior Surgical Score; PCI: Peritoneal Carcinomatosis Index. p values calculated by Fisher's exact test or χ^2 test. For continuous variables where only group medians were available, p values were derived from published matched-cohort data or reported as calculated by propensity-matching algorithm.</i>			

Perioperative outcomes

Complete cytoreduction (CC-0) was achieved in all cases. Median operative time including HIPEC perfusion was significantly shorter in the LAP group (240 vs. 312 min, $p = 0.0045$), as was intraoperative blood loss (100 vs. 300 mL, $p = 0.0188$). Peak intraoperative glucose (209 vs. 222.5 mg/dL, $p = 0.225$) and maximum intraoperative temperature (37.7 vs. 37.95°C, $p = 0.245$) were comparable. The number of intestinal anastomoses did not differ between groups (median 0 vs. 0, $p = 0.406$), although open procedures showed a wider range (0–3 vs. 0–1), suggesting a higher frequency of multi-visceral resections in the open cohort.

Peritonectomy rates were similar: right diaphragmatic 21.1% vs. 15.8% ($p = 1.000$); left diaphragmatic 5.3% vs. 10.5% ($p = 0.637$); pelvic 26.3% vs. 21.1% ($p = 1.000$). No significant difference was found in IPC protocol distribution (oxaliplatin-based vs. non-oxaliplatin, $p = 0.709$).

Median hospital stay was significantly shorter in the LAP group (4 vs. 8 days, $p = 0.0049$). ICU stay was identical in both groups (median 1 day). Overall morbidity was significantly lower following laparoscopic CRS–HIPEC (26.3% vs. 61.3%, RR 0.43, 95% CI 0.20–0.91, $p = 0.0215$). Major complication rates (CD $\geq$ III) were similar between groups (5.3% vs. 5.9%, $p = 1.000$). No 30-day postoperative mortality occurred in either group. Perioperative outcomes are shown in Table 2.

Table 2
Perioperative characteristics

Variable	LAP n = 19	OPEN n = 38	p value
Operative time, median (IQR) (min)	240 (210–265)	312 (270–360)	0.0045
Blood loss, median (IQR) (mL)	100 (50–200)	300 (150–500)	0.0188
Peak glucose, median (mg/dL)	209	222.5	0.225
Max intraoperative temperature, median (°C)	37.7	37.95	0.245
Right diaphragmatic peritonectomy, n (%)	4 (21.1%)	6 (15.8%)	1.000
Left diaphragmatic peritonectomy, n (%)	1 (5.3%)	4 (10.5%)	0.637
Pelvic peritonectomy, n (%)	5 (26.3%)	8 (21.1%)	1.000
Total peritonectomies, n	10	18	0.783
Bowel anastomoses, median (range)	0 (0–1)	0 (0–3)	0.406
ICU stay, median (IQR) (days)	1 (0–1)	1 (1–1)	0.709
Hospital stay, median (IQR) (days)	4 (3–5)	8 (6–11)	0.0049
Any complication, n (%)	5 (26.3%)	23 (61.3%)	0.0215
Major complication (CD $\geq$ III), n (%)	1 (5.3%)	2 (5.9%)	1.000
<i>ICU: Intensive Care Unit; CD: Clavien–Dindo classification; IQR: interquartile range. p values by Fisher’s exact test or Mann–Whitney U test. Total peritonectomies reflect procedures performed; patients without peritoneal disease in a given region did not require peritonectomy.</i>			

Follow-up and survival

Median follow-up was 18.9 months in the LAP group and 22.9 months in the OPEN group ($p = 0.785$). Patients in the LAP group showed a significantly higher rate of complete disease control at last follow-up (84.2% vs. 65.8%, RR 1.28, 95% CI 1.00–1.64, $p = 0.047$). The proportion of patients alive at last follow-up was higher in the LAP group (94.7% vs. 78.9%), although this difference did not reach statistical significance ($p = 0.247$). Survival outcomes are shown in Table 3. Kaplan-Meier survival curves are shown in Fig. 1.

Table 3
Follow-up and survival outcomes

Variable	LAP n = 19	OPEN n = 38	p value
Follow-up, median (months)	18.9	22.9	0.785
Alive without disease, n (%)	16 (84.2%)	25 (65.8%)	0.047
Alive with disease, n (%)	2 (10.5%)	5 (13.2%)	1.000
Dead of disease, n (%)	1 (5.3%)	7 (18.4%)	0.247
Dead of other cause, n (%)	0 (0%)	1 (2.6%)	1.000
Alive at last follow-up (overall survival), n (%)	18 (94.7%)	30 (78.9%)	0.247
<i>p values by Fisher's exact test. Overall survival defined as proportion of patients alive at last follow-up.</i>			

Discussion

This propensity score-matched cohort study demonstrates that laparoscopic CRS-HIPEC is a feasible and safe approach for carefully selected patients with colorectal and appendiceal peritoneal metastases. Compared with open CRS-HIPEC, the laparoscopic approach was associated with significantly shorter operative time, lower intraoperative blood loss, shorter hospital stay, and lower overall postoperative morbidity, while maintaining comparable rates of major complications, complete cytoreduction, and short-term oncologic outcomes.

Minimally invasive CRS-HIPEC has gained increasing attention due to potential advantages including improved visualisation, reduced surgical trauma, and faster postoperative recovery. However, this technique remains highly demanding and dependent on appropriate patient selection, surgical expertise, and institutional experience [6, 7]. The learning curve and procedure volume are critical considerations when implementing laparoscopic CRS-HIPEC programmes. All procedures in the present series were performed by a specialised team with extensive experience in advanced laparoscopic and robotic colorectal, appendiceal, and peritoneal malignancy surgery, which likely contributed to the favourable perioperative outcomes observed.

Arjona-Sánchez et al. reported one of the largest international multicentre series of laparoscopic CRS-HIPEC, comprising 143 patients with limited PM predominantly of appendiceal or colorectal origin, supporting the feasibility and safety of the laparoscopic approach in selected low-PCI cases [10]. A recent systematic review corroborates these findings while highlighting significant limitations including heterogeneity, small sample sizes, and the absence of prospective comparative trials [5]. Our cohort is comparable in size to the largest single-centre experiences reported to date. Our findings are consistent with those of Bortoli et al., who also observed improved short-term outcomes after laparoscopic CRS-HIPEC in low-PCI patients [11], and with recent propensity-matched analyses showing similar surgical complexity between approaches [11, 12, 17].

The reduction in overall morbidity (RR 0.43, 95% CI 0.20–0.91) observed in the laparoscopic group aligns with the existing literature [16, 18]. Although major complication rates were equivalent between approaches, the reduction in minor morbidity and hospital stay has relevant implications for patient recovery and resource utilisation. Open procedures showed a wider anastomosis range (0–3 vs. 0–1), suggesting a higher frequency of multi-visceral resections and potentially greater surgical complexity in the open cohort despite comparable PCI values.

The shorter operative time in the laparoscopic group may partly reflect the absence of xipho-pubic laparotomy closure and, in earlier cases, the use of a short-duration oxaliplatin-based HIPEC protocol. Notably, no significant differences were observed in IPC regimen distribution between groups. Oxaliplatin-based HIPEC was abandoned in favour of Mitomycin C–based protocols following the results of the PRODIGE 7 trial [9].

The use of a minimally invasive approach may have implications extending beyond the index procedure. A prior laparoscopic intervention might reduce surgical complexity in subsequent operations for peritoneal recurrence due to a potentially reduced burden of intra-abdominal adhesions. The Prior Surgical Score (PSS) has been identified as an important prognostic factor: higher scores are associated with increased adhesions, lower complete cytoreduction rates, and worse overall survival [15]. This potential long-term benefit warrants prospective evaluation.

Although disease-free status and overall survival appeared more favourable in the laparoscopic cohort, these findings must be interpreted with caution given the shorter follow-up duration (18.9 vs. 22.9 months) and retrospective study design. Survival differences should be considered hypothesis-generating. Kaplan–Meier analysis with individual patient survival data would strengthen these observations.

This study has several limitations: its retrospective design, a relatively small sample size in the laparoscopic group ($n = 19$), absence of individual-level data for certain continuous variables, and potential residual confounding despite propensity score matching. The single-centre design may limit generalisability to centres with less experience in advanced laparoscopic oncology. Nevertheless, the use of a prospectively maintained database and 1:2 propensity score matching strengthens the validity of the comparative analysis.

Conclusion

Laparoscopic CRS–HIPEC is a safe and feasible option in carefully selected patients with low-PCI colorectal and appendiceal peritoneal metastases, when performed in high-volume, experienced centres. The laparoscopic approach reduces intraoperative blood loss, hospital stay, and overall postoperative morbidity without increasing major complications or compromising short-term oncologic outcomes. Prospective, multicentre studies with long-term follow-up are warranted to confirm these findings and refine patient selection criteria.

Declarations

Disclosures

Silvia Valverde, Anaïs Besa, Romina Pena, Sara Tavares, Ana Otero, Raquel Bravo, and Miguel Pera have no conflicts of interest to disclose.

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Study registration

This study was not prospectively registered. It was conducted and reported in accordance with the STROCSS 2021 criteria for observational surgical studies.

Ethics approval

This study was conducted in accordance with the Declaration of Helsinki and approved by the Comité de Ética de la Investigación con Medicamentos (CEIm) del Hospital Clínic de Barcelona (Reg. HCB/2021/1212; acta 21/2021; 02/12/2021), in compliance with EMA/CHMP/ICH/135/1995 guidelines. All patients provided written informed consent prior to participation. All patients provided written informed consent for surgical procedures and the use of their anonymized data for research purposes.

Author contributions

Silvia Valverde: Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft. Anaïs Besa, Romina Pena, Sara Tavares, Raquel Bravo: Data curation, Investigation, Writing – review & editing. Ana Otero: Formal analysis, Writing – review & editing. Miguel Pera: Supervision, Writing – review & editing, Project administration.

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Figures

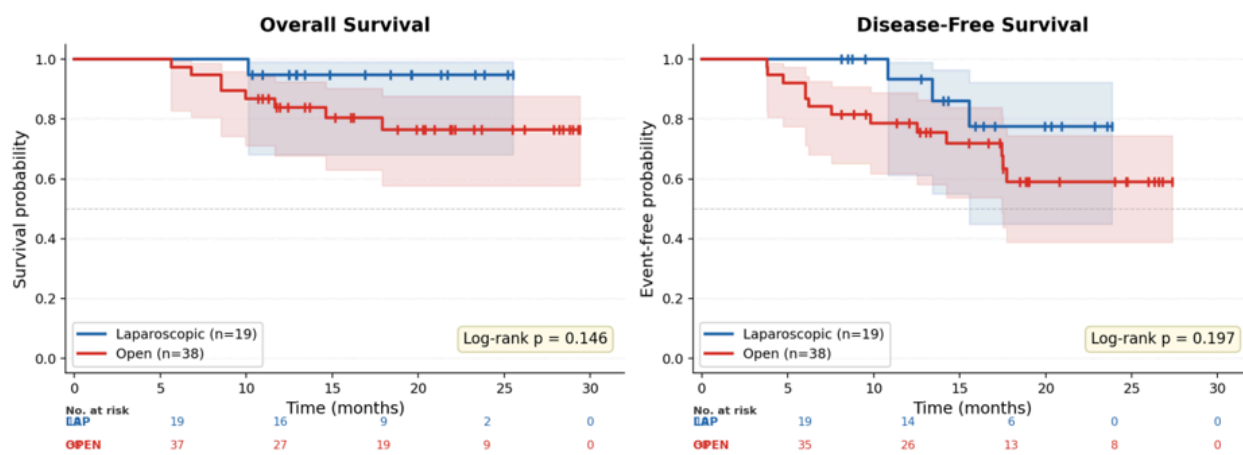


Figure 1

Kaplan-Meier survival curves