Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy in Patients With Liver Involvement

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Background: We examined outcomes of patients undergoing cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) combined with liver resection.

Methods: All patients undergoing CRS/HIPEC between 2007 and 2014 were retrospectively reviewed: patients who underwent synchronous liver resection (group 1) were compared with those who did not (group 2) in terms of perioperative and long-term results.

Results: Group 1 included 103 patients with colorectal cancer (CRC, n = 28), appendiceal cancer (n = 34), and other malignancies. Compared with group 2 (n = 166), group 1 had higher number of organs resected, increased intraoperative blood loss, and longer hospital stay (all $P \leq 0.004$) but similar major morbidity (24.3% vs. 18.1%, $P = 0.22$) and perioperative mortality rates. Two patients from group 1 developed liver resection-related complications. A comparison between patients who underwent parenchymal liver resection (n = 42) and matched pairs from group 2 with similar extent of cytoreduction did not yield significant differences in morbidity/mortality. CRC patients from group 1 had poorer median overall survival (45.1 vs. 73.5 months from stage IV diagnosis, $P = 0.009$).

Conclusions: Liver involvement denotes high peritoneal carcinomatosis burden, which often requires resection of multiple organs in order to achieve optimal cytoreduction. However, liver resection-related morbidity is low and overall morbidity/mortality rates are comparable to other extensive CRS/HIPEC procedures.

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KEY WORDS: cytoreductive surgery; hyperthermic intraperitoneal chemotherapy; liver resection; hepatectomy

INTRODUCTION

The presence of intra-parenchymal liver metastasis has traditionally been regarded as a contraindication for cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) [1]. Over the last decade, as surgical resection of isolated colorectal cancer (CRC) liver metastases has become more widely accepted, several studies describing a synchronous resection of liver and peritoneal metastases (with or without HIPEC) have emerged and demonstrated that the survival benefit associated with the combined procedure is similar to that seen in patients without liver metastases undergoing CRS/HIPEC [2–6]. In 2008, a consensus statement on the loco-regional treatment of CRC with peritoneal dissemination stated that achieving a complete cytoreduction is feasible in cases where up to three small, resectable parenchymal hepatic metastases are present [7].

Although the liver is a frequent site for peritoneal and hematogenous metastases, reports on liver resection as part of CRS/HIPEC are scarce and the impact of liver resection on CRS/HIPEC short- and long-term outcomes remains unclear. We examine the perioperative and long-term results in patients with liver involvement undergoing CRS/HIPEC at a single tertiary referral institution.

METHODS

Data were obtained from a prospectively collected database maintained between 3/2007 and 7/2014. All patients undergoing CRS/HIPEC with therapeutic intent were included in this IRB approved study. The cohort was divided into two groups: patients who underwent synchronous liver resection (group 1) and those who did not (group 2); perioperative and long-term results were compared between groups.

Our preoperative planning and operative technique have been previously described [8,9]. Briefly, diagnostic laparoscopy was performed routinely when feasible and converted to laparotomy when a complete cytoreduction was deemed possible. The peritoneal cancer index (PCI) was recorded according to the Sugarbaker classification [10]. Cytoreduction was then performed, which consisted of resection of the primary tumor (if not previously resected), omentectomy, resection of involved intra-abdominal organs, and stripping of involved parietal peritoneum surfaces. The spectrum of liver resections performed as part of cytoreduction ranged from superficial stripping of the liver capsule to major anatomical hepatic resections. All liver resections were performed by the same surgical oncology team who performed the CRS/HIPEC. The Pringle maneuver was used during complicated parenchymal resections. Hemostasis of the raw surface of the liver was achieved by using

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electrocautery, Gelfoam–Thrombin or argon beam coagulator, as needed.

Following cytoreduction, the completeness of cytoreduction (CC) score was recorded according to the Sugarbaker classification [10,11]; complete cytoreduction was defined as CC score $\leq$1. HIPEC was then delivered via the closed abdomen technique, using Mitomycin C as the most common chemotherapeutic agent (88%). Following the administration of HIPEC, gastrointestinal anastomoses were created.

The types of liver involvement (peritoneal vs. hematogenous metastasis) and liver resection (superficial vs. parenchymal) were classified according to operative and pathology reports. The estimated volume of resected liver was calculated according to gross pathology reports. Any resection with depth $\geq$10 mm beyond the liver capsule was considered parenchymal, whether performed for hematogenous metastasis or deep peritoneal invasion; based on our experience, 10 mm was the minimal depth required to perform non-anatomical (wedge) resection. In accordance with previously published studies [12,13], superficial resection, defined as resection depth $<$10 mm beyond the liver capsule, was included in the liver resection group. Major hepatectomy was defined as resection of $\geq$3 liver segments. Major postoperative morbidity was defined as Clavien–Dindo classification III–V [14].

Data were analyzed with SPSS program version 22 (Chicago, IL). Categorical data are expressed as percentages and continuous data are expressed as mean $\pm$ standard deviation. The Student *t*-test and Mann–Whitney test were used to compare continuous variables. Categorical variables were compared by the χ^2 test or Fisher's exact test. For the matched pair analysis, variables were compared by the paired *t*-test, McNemar's test, or Wilcoxon signed-rank test, as applicable; matching criteria were number of resected organs, presence of bowel anastomoses, and diaphragmatic resection. Survival analyses were restricted to patients with CRC or high grade appendiceal tumors (HGA) and calculated using the Kaplan–Meier method; subgroups were compared with the log-rank test. Overall survival (OS) was calculated from the date of stage IV diagnosis and progression free survival (PFS) was calculated from the date of CRS/HIPEC. A *P*-value of $<$0.05 was defined as significant.

RESULTS

Between 3/2007 and 7/2014, a total of 257 patients underwent 269 CRS/HIPEC procedures. Group 1 included 103 CRS/HIPEC procedures (38%) performed in 101 patients with primary diagnoses of CRC (27%), HGA (33%), low-grade appendiceal mucinous neoplasm (13%), ovarian cancer (6%), gastric cancer (5%), mesothelioma (5%), and other malignancies (11%) including hepatocellular carcinoma (n = 3), cholangiocarcinoma (n = 2), pancreatic cancer (n = 2), gallbladder cancer (n = 1), melanoma (n = 1), mullerian tumor (n = 1), and teratoma (n = 1). The type of liver involvement was classified as peritoneal metastasis in most of the cases (n = 84, 82%); in 14 cases (14%), the liver was involved by hematogenous metastasis, mainly from colorectal origin (n = 9). There were a few cases in which the liver was involved by direct local invasion of an intra-abdominal tumor (n = 2) or by a primary tumor of the liver (cholangiocarcinoma: n = 2; hepatocellular carcinoma: n = 1). Most liver resections (55.3%) in group 1 were superficial, whereas 46 procedures (44.7%) consisted of parenchymal resection (Fig. 1).

Group 2 consisted of 156 patients who underwent 166 CRS/HIPEC procedures. Preoperative and intra-operative characteristics of both study groups are presented in Table I. Preoperative variables were not significantly different between the groups, except for the rate of previous abdominal surgery, which was significantly higher in group 2. Group 1 had significantly longer duration of surgery, increased intraoperative blood loss, higher number of organs resected and higher PCI scores (all $P \leq 0.004$). In addition, the prevalence of concomitant resection of the diaphragm, gallbladder, distal pancreas, spleen, and stomach was significantly higher in group 1. There was no significant difference between the groups in the rate of complete cytoreduction. Out of 28 CRC patients in group 1, 25 patients (89.3%) had received prior systemic chemotherapy (1 treatment line: n = 14; 2 lines: n = 8; $\geq$3 lines: n = 3).

Postoperative outcomes are presented in Table II. The length of hospital stay and the rate of ICU admissions were significantly higher in group 1. The rate of overall 30-day morbidity (Clavien–Dindo I–V) was higher in group 1, but this difference only approached statistical significance ($P = 0.06$). Major 30-day morbidity (group 1: 24.3% vs. group 2: 18.1%, $P = 0.22$) and 90-day mortality (group 1: 5.8% vs. group 2: 6.7%, $P = 0.76$) were not significantly different between groups. The rate of overall and major respiratory complications was significantly higher in group 1. Other complications did not differ significantly between the groups. There were only two documented cases of liver resection-related complications in group 1: one case of bile leak following right hepatectomy and another case of liver abscess following non-anatomic parenchymal resection. Both cases were treated with interventional radiology.

In order to determine if the adverse intraoperative and postoperative outcomes observed in group 1 are related to liver resection or to multi-visceral resection, a matched-pair analysis was conducted. Fourty-two patients who underwent parenchymal liver resection were matched with patients who did not undergo liver resection in terms of the extent of cytoreduction (Table III). The mean duration of surgery, mean

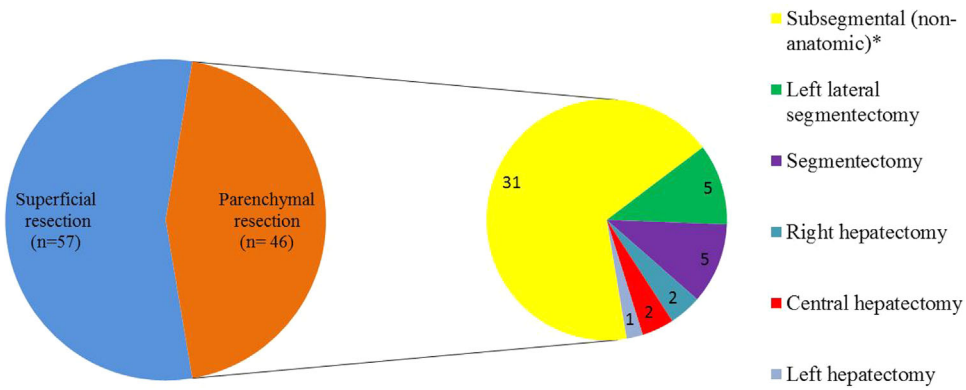

Fig. 1. Types of liver resection procedures performed in group 1 (n = 103). The median volume of liver resected during parenchymal and superficial resection procedures was 83.1 (3.2–1764) ml and 3.0 (0.02–36.7) ml, respectively. *radiofrequency ablation was added in one case.

TABLE I. Preoperative and Intraoperative Characteristics

	Group 1: CRS/HIPEC with liver resection (n = 103)	Group 2: CRS/HIPEC without liver resection (n = 166)	*P*-value
Preoperative			
Male, n (%)	48 (46.6)	63 (38.0)	0.16
Age, mean (SD), years	54.5 (11.3)	55.0 (12.3)	0.73
Presence of comorbidities*, n (%)	37 (35.9)	60 (36.1)	0.97
ASA score >3, n (%)	10 (9.7)	18 (10.8)	0.76
ASA score, median (range)	3 (2–4)	3 (0–4)	0.89
Primary tumor site, n (%)			
Colorectal	28 (27.2)	54(32.5)	0.43
High-grade appendiceal tumor	34 (33.0)	42 (25.3)	
Low-grade appendiceal tumor	13 (12.6)	17 (10.2)	
Other**	28 (27.2)	53 (31.9)	
Number of systemic chemotherapy lines given prior to CRS/HIPEC, n(%)			
0	43 (41.7)	72 (43.4)	0.67
1	37 (35.9)	64 (38.6)	
2	16 (15.5)	24 (14.5)	
≥3	7 (6.8)	6 (3.6)	
Previous abdominal surgery, n (%)	64 (62.1)	132 (79.5)	**0.002**
Intra-operative			
Duration of surgery, mean (SD), minutes	379.3 (108.9)	316.9 (122.7)	**<0.001**
EBL, mean (SD), cc	761.3(880.8)	453.5(826.9)	**0.004**
Patients receiving blood transfusions, n (%)	45 (43.7)	41 (24.7)	**0.001**
Concomitant organs resected, n (%)			
Diaphragm	77 (74.8)	35 (21.1)	**<0.001**
Gallbladder	31 (30.1)	13 (7.8)	**<0.001**
Distal pancreas	18 (17.5)	5 (3.0)	**<0.001**
Spleen	50 (48.5)	16 (9.6)	**<0.001**
Stomach	18 (17.5)	15 (9.0)	**0.04**
Small bowel	27 (26.2)	49 (29.5)	0.55
Colon/rectum	57 (55.3)	61 (36.7)	**0.003**
Creation of ≥1 GI anastomosis, n(%)	59 (57.3)	83 (50.0)	0.24
PCI score, median (range)	17.5 (3–35)	10 (0–39)	**<0.001**
Number of organs resected, median (range)	5 (1–10)	2 (0–9)	**<0.001**
CC score 0/1, n(%)	81 (83.5)	117 (81.8)	0.74
CC score > 1, n(%)	16 (16.5)	26 (18.2)	

CRS/HIPEC, cytoreductive surgery and hyperthermic intraperitoneal chemotherapy; ASA, American society of anesthesiologists; EBL, estimated blood loss; GI, gastrointestinal; PCI, peritoneal carcinomatosis index; CC, completeness of cytoreduction.

*Presence of comorbidities was defined as having at least one of the following: hypertension, diabetes, or chronic heart/lung/liver/kidney disease.

**Other malignancies: ovarian cancer, gastric cancer, mesothelioma, small bowel adenocarcinoma, hepatocellular carcinoma, sarcoma, cholangiocarcinoma, pancreatic cancer, endometrial cancer, gallbladder cancer, melanoma, mullerian tumor, breast cancer, and teratoma.

The bold values are significant *P* values.

TABLE II. Postoperative Outcomes

	Group 1: CRS/HIPEC with liver resection (n = 103)	Group 2: CRS/HIPEC without liver resection (n = 166)	*P*-value
Any 30-day morbidity (Clavien–Dindo I–V)			
Overall patients, n (%)	61 (59.2)	79 (47.6)	0.06
Any respiratory complications*, n (%)	23 (22.3)	21 (12.7)	**0.04**
Pleural effusion, n (%)	13 (12.6)	11 (6.6)	0.09
Any wound complications, n (%)	8 (7.7)	19 (11.4)	0.33
Paralytic ileus, n (%)	14 (13.6)	22 (13.2)	0.94
Transient neutropenia, n (%)	8 (7.7)	14 (8.4)	0.85
Major 30-day morbidity (Clavien–Dindo III–V)			
Overall patients, n (%)	25 (24.3)	30 (18.1)	0.22
Major respiratory complications, n (%)	12 (11.7)	8 (4.8)	**0.038**
Respiratory failure**, n (%)	9 (8.7%)	3 (1.8%)	**0.012**
Severe Pleural effusion***, n (%)	5 (4.9)	2 (1.2)	0.11
Intra-abdominal abscess/leak, n (%)	13 (12.6)	15 (9.0)	0.35
Pulmonary embolus, n (%)	3 (2.9%)	4 (2.4%)	1.0
Myocardial infarct, n (%)	2 (1.9)	0 (0)	0.15
Major wound complications, n (%)	4 (3.9)	5 (3.0)	0.73
90-day mortality, n (%)	6 (5.8)	11 (6.7)	0.76
In-hospital mortality, n (%)	3 (2.9)	4 (2.4)	0.80
90-day re-operation, n (%)	6 (5.8)	20 (12.2)	0.09
Length of hospital stay, days, median (range)	8 (3–99)	6 (2–101)	**0.002**
ICU stay, days, median (range)	0 (0–62)	0 (0–23)	**0.02**
ICU admissions, n (%)	23 (22.3)	19 (11.5)	**0.02**

CRS/HIPEC, cytoreductive surgery and hyperthermic intraperitoneal chemotherapy; ICU, intensive care unit.

*Respiratory complications: pleural effusion, pneumonia, pneumothorax, pulmonary embolism, and respiratory failure.

**Respiratory failure: re-intubation or failure to wean from mechanical ventilation.

***Severe pleural effusion: requiring insertion of a chest tube or thoracocentesis.

The bold values are significant *P* values.

TABLE III. Matched Pair Analysis of Patients Who Underwent Parenchymal Liver Resection (Median Volume Resected: 83.1 ml) Versus Patients Who Did Not Undergo Liver Resection

	CRS/HIPEC with parenchymal liver resection (n = 42)	CRS/HIPEC without liver resection (n = 42)	*P*-value
Male, n (%)	19 (45.2)	19 (45.2)	1.0
Age, mean (SD), years	54.2 ± 12.2	55.1 ± 14.7	0.78
Primary tumor site, n(%)			
Colorectal/appendiceal	29 (69.0)	24 (57.1)	0.42
Other	13 (31.0)	18 (42.9)	
Duration of surgery, mean (SD), minutes	408.4 ± 110.2	379.5 ± 121.2	0.15
EBL, mean (SD), cc	841.4 ± 820.4	841.2 ± 1032.6	0.99
Concomitant diaphragm resection, n (%)	28 (66.7)	27 (64.3)	1.0
Creation of ≥1 GI anastomosis, n (%)	21 (50.0)	21 (50.0)	1.0
Number of organs resected*, median (range)	2 (0–7)	2.5 (0–7)	0.80
Overall 30-day morbidity, n (%)	30 (71.4)	27 (64.3)	0.65
Major 30-day morbidity, n (%)	13 (31.0)	10 (23.8)	0.61
Length of hospital stay, days, median (range)	9 (3–99)	8 (3–101)	0.78
ICU admissions, n (%)	13 (31.0)	11 (26.2)	0.79
90-day mortality, n (%)	3 (7.1)	6 (14.3)	0.51

Matching criteria were number of resected organs*, presence of bowel anastomoses, and diaphragmatic resection.
CRS/HIPEC, cytoreductive surgery and hyperthermic intraperitoneal chemotherapy; EBL, estimated blood loss; GI, gastrointestinal; ICU, intensive care unit.
*Excluding the liver, omentum, and peritoneum.

estimated blood loss, median length of hospital stay, and morbidity/mortality rates were not significantly different between the matched groups.

The median follow-up period was 18.2 months from the date of CRS/HIPEC and 31.3 months from the date of stage IV diagnosis. Median OS was 73.5 months in CRC patients without liver involvement and was 45.1 months for those with liver involvement ($P = 0.009$, Fig. 2a). CRC patients with liver involvement had higher median PCI (18.5 vs. 7, $P < 0.001$) and higher proportion of incomplete cytoreduction (25.0% vs. 9.3%, $P = 0.056$) when compared with patients without liver involvement; other unfavorable tumor characteristics such as the proportion of positive lymph node status (78.3% vs. 75.0%, $P = 0.76$) and high tumor grade (42.9% vs. 40.7%, $P = 0.98$) were not significantly different, as well as the number of systemic chemotherapy lines given prior to CRS/HIPEC in each group (no prior chemotherapy: 10.7% vs. 13%; one chemotherapy line: 50.0% vs. 59.3%; ≥2 lines: 39.3% vs. 27.8%, $P = 0.57$).

In patients with HGA, the corresponding OS difference was statistically insignificant (group 1: median OS was not reached vs. group 2: 42.0 months, $P = 0.54$, Fig. 2b). Median PFS did not differ significantly between groups when calculated for CRC patients (group 1: 17.3 months vs. group 2: 13.2 months, $P = 0.89$) and HGA patients (group 1: 13.1 months vs. group 2: 14.0 months, $P = 0.37$).

Overall, 18 CRC patients underwent CRS/HIPEC with synchronous (n = 9) or metachronous (n = 9) resection of hematogenous liver metastases during the follow up period. The median timing of metachronous resection was 3 months before CRS/HIPEC (range: 32.1 months before CRS/HIPEC to 17.7 months after CRS/HIPEC). The median OS of this subgroup, measured from the date of stage IV diagnosis, was not significantly different from that of CRC patients with peritoneal carcinomatosis (PC) alone undergoing CRS/HIPEC (50.9 vs. 59.6 months, respectively, $P = 0.64$). Survival was longer than 2 years in 10 of these patients, with the longest follow up period being 71 months.

DISCUSSION

Since the first liver metastasectomy was performed by Cattell more than 70 years ago, surgical resection of CRC metastases confined to the liver has evolved into the standard of care. However, in patients with PC the presence of parenchymal liver involvement has traditionally been regarded as a contraindication for CRS/HIPEC. It was once believed that synchronous presentation of both modes of cancer dissemination—loco-regional and hematogenous—was associated with poor treatment outcome that does not justify the operative morbidity of CRS/HIPEC [1]. During the last decade, this assumption was repeatedly challenged by several studies reporting a simultaneous

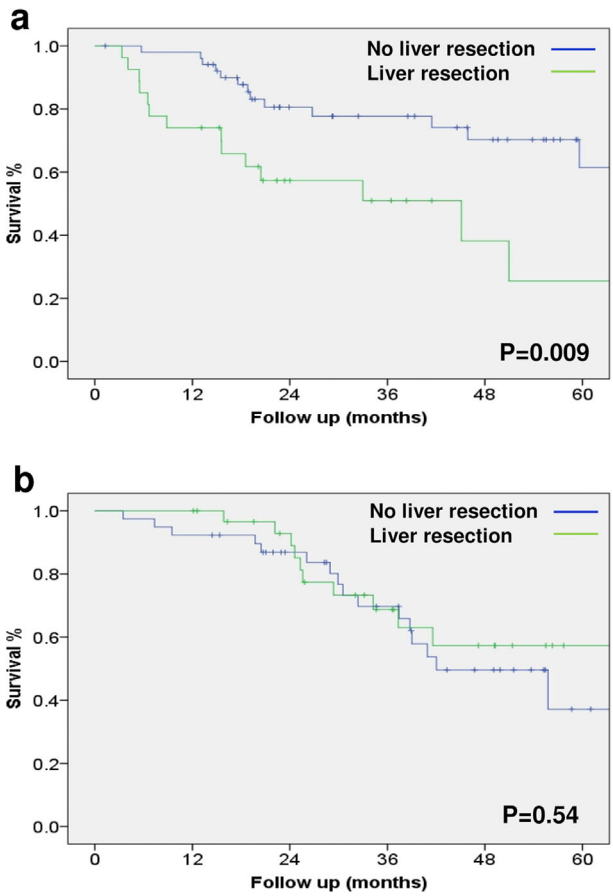

Fig. 2. Overall survival analysis of patients undergoing CRS/HIPEC: (**a**) Patients with CRC. (**b**) Patients with HGA. CRS/HIPEC, cytoreductive surgery and hyperthermic intraperitoneal chemotherapy; CRC, colorectal cancer; HGA, high grade appendiceal tumors.

resection of PC and hematogenous liver metastases, mainly in CRC patients [4–6]. A recently published meta-analysis suggested that CRC patients undergoing CRS/HIPEC combined with resection of liver metastases show a tendency towards increased median overall survival when compared to treatment with modern systemic chemotherapy alone [15]. Very few studies have addressed the impact of non-hematogenous liver involvement on CRS/HIPEC outcomes [12,13].

Our primary aim was to examine the effect of liver resection procedures performed as part of CRS/HIPEC on perioperative outcomes. In this regard, it is one of the largest series published to date. Group 1 represents a large heterogeneous cohort of patients with various types of liver involvement. Similar to previous studies [12,13] the liver was most commonly involved by peritoneal metastases that required superficial or subsegmental resection. This type of liver involvement was associated with high tumor burden and a resultant multi-organ resection, suggesting that patients with PC requiring liver resection usually present with more disseminated disease involving additional organs and peritoneal surfaces; this is also evidenced by the higher rates of concomitant adjacent organ resections observed in group 1. Our matched pair analysis suggests that the increased intra-operative blood requirements and the longer lengths of hospital stay and duration of surgery, which were demonstrated in group 1 are likely related to the more extensive cytoreduction performed in this group rather than liver resection itself.

Importantly, in spite of the fact that cytoreduction was much more aggressive in group 1, we found that liver resection procedures in combination with CRS/HIPEC are safe and are not associated with excessive major morbidity or mortality. The incidence of major postoperative morbidity in group 1 (24.3%) is comparable to that found in another similar study on CRS/HIPEC combined with hepatobiliary procedures (33%,[12]) as well as to the 12–66% reported in other large CRS/HIPEC series [16]. Respiratory complications were the only postoperative morbidity whose incidence was higher among patients with liver involvement. We hypothesize that this finding is related to the higher prevalence of concomitant diaphragmatic resections performed in group 1, as many of the patients who underwent diaphragmatic resection were diagnosed with respiratory complications including pleural effusion [8]. Similar to the study by Glockzin et al. in which the rate of specific postoperative complications attributable to hepatobiliary procedures was only 4.8% [12], we also found a low rate of liver resection-related morbidity (2 out of 103 patients, 1.9%).

Kianmanesh et al. suggested that in cases where hematogenous liver metastases require major hepatectomy, especially after previous systemic chemotherapy treatment, liver resection should be delayed and performed several months following CRS/HIPEC in a two-step fashion, due to morbidity-mortality considerations [2]. Although it is not appropriate to make strong recommendations based on a small sample size, our study suggests that the need for parenchymal liver resection should not be a contraindication to CRS/HIPEC combined with concurrent hepatectomy in well-selected patients. Nevertheless, given the limited number of major hepatectomies ($n = 5$) performed in our cohort, further, larger studies are needed to confirm safety of CRS/HIPEC combined with resection of ≥ 3 liver segments.

Our analysis demonstrated that the median overall survival in CRC-PC patients who underwent CRS/HIPEC with liver resection (45.1 months) is comparable to that reported in other large CRS/HIPEC series (16–62.7 months [17]) and may be better than that achieved with modern systemic chemotherapy alone (10.4–23.9 months [15]). In this regard, it is important to emphasize that most patients in group 1 had received prior systemic chemotherapy before the CRS/HIPEC procedure, therefore the median OS measured in this group (from the date of stage IV diagnosis) may reflect the cumulative effect of CRS/HIPEC and modern systemic chemotherapy on oncological outcomes. Compared to CRC-PC patients without liver involvement, the overall survival of those with liver involvement was significantly unfavorable; this survival difference is likely attributable to the more disseminated peritoneal disease observed in group 1 as well as the higher proportion of incomplete cytoreduction, since these two factors have been recognized as the most important prognostic predictors following CRS/HIPEC. As we gained experience with CRS/HIPEC procedures, we have adopted several inclusion criteria for CRS/HIPEC in patients with PC and liver involvement: patients with CRC were typically required to undergo neoadjuvant systemic chemotherapy with demonstration of a progression-free interval of at least 3 months; patients were required to be surgical candidates with good performance status; as described in the literature, only patients with PCI scores <21 [18,19] were considered likely to be optimally cytoreduced and staged diagnostic laparoscopy was liberally used to assess whether this would be feasible [20]. Surgery was infrequently employed in patients with high-volume peritoneal disease ($PCI \geq 21$), particularly in the setting of concurrent large hepatic tumor burden, and most of these patients were operated on during the early study period, which reflects our learning curve in terms of patient selection.

Although limited by small number of patients, our analysis yielded similar overall survival periods for CRC patients with hematogenous liver metastases and those with PC alone. This finding is consistent with previous reports [2,5,6] and highlights the value of CRS/HIPEC combined with parenchymal liver resection. Furthermore, long term survival periods ($\geq$24 months) were achieved in some of these patients. In contrast, the reported median survival achieved by palliative chemotherapy in patients with combined liver metastasis and PC is only 12 months [21]. Long term surviving patients in our cohort had a low-moderate tumor burden (median PCI score = 10), which reinforces the importance of careful preoperative patient selection for this combined procedure. At our institution, each case of hematogenous liver metastasis is discussed in a multidisciplinary team meeting; PC burden, number and size of liver metastases are considered. Referral to CRS/HIPEC with liver metastasectomy is decided according to each individual case.

Our study has several limitations. Firstly, our group of patients with liver involvement was heterogeneous and was composed of patients with different types of primary malignancies and liver involvement (PC vs. hematogenous); accordingly, we focused on perioperative outcomes and survival analysis was calculated separately for small subgroups. Secondly, there was an unavoidable element of selection bias incorporated in the outcomes, as the two main study groups were unbalanced in terms of peritoneal tumor burden and extent of CRS/HIPEC. Additionally, some patients were lost to follow up, as our institution is a tertiary referral center.

In conclusion, the liver is frequently involved in patients with PC. Liver involvement denotes high tumor burden, which often requires resection of multiple upper-abdominal organs in order to achieve optimal cytoreduction, and is associated with unfavorable survival in CRC patients. However, liver resection-related morbidity is low and overall morbidity/mortality rates are comparable to other extensive CRS/HIPEC procedures. In addition, CRS/HIPEC even in the presence of liver involvement offers certain patients the potential for long-term survival.

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SYNOPSIS

This study is a retrospective analysis of perioperative and long-term outcomes in patients undergoing liver resection as part of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy procedures.