Asian Journal of Surgery 47 (2024) 296–302

Contents lists available at ScienceDirect

Asian Journal of Surgery

journal homepage: www.e-asianjournalsurgery.com

Original Article

Is cytoreductive surgery and hyperthermic intraperitoneal chemotherapy still beneficial in patients with colorectal peritoneal metastasis who undergoing palliative chemotherapy?

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ARTICLE INFO

Article history:
Received 16 March 2023
Received in revised form
5 July 2023
Accepted 22 August 2023
Available online 28 August 2023

Keywords:
Colorectal neoplasm
Cytoreductive surgery
Intraperitoneal chemotherapy
Peritoneal carcinomatosis

ABSTRACT

Background: With a 5-year overall survival of less than 5%, colorectal peritoneal metastasis (CPM) patients are often managed with palliative chemotherapy (CTx). In the past few decades, cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) has been introduced as a possible curative treatment for highly selective CPM patients. We share our experience of CRS and HIPEC given the unique characteristics of the medical system and the benefit of CRS and HIPEC in palliative setting.
Methods: From April 2017 to October 2021, CPM patients who underwent CRS and HIPEC were analyzed. Patients were allocated into perioperative and palliative CTx arm based on the duration between initial diagnosis of CPM to undergoing CRS and HIPEC of 6 months. Data including perioperative parameters, postoperative outcomes, and survival were analyzed with a median follow-up of 28.5 months.
Results: Twenty-six CPM patients underwent CRS and HIPEC. Mean time from diagnosis of CPM to CRS and HIPEC was 5.5 months with 14 patients in the perioperative arm and 12 patients in the palliative arm. Perioperative group showed a longer RFS of 13.5 months compared to 8 months in the palliative group. Median overall survival of palliative group was 41.50 months, and 18 patients among all groups are alive at the time of this report.
Conclusion: CRS and HIPEC could be a treatment option for a carefully selected CPM patients performed by experienced surgeons. Overall survival of 41.50 months in palliative group compared to 16.8 months from conventional systemic CTx supports CRS and HIPEC even in palliative patients.

1. Introduction

Colorectal peritoneal metastasis (CPM) occurs in approximately 10–15% and its prognosis is worst among stage IV colorectal cancer. With a 5-year overall survival of less than 5%, CPM patients are often managed with palliative chemotherapy. In the past decade, cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) have been introduced as possible curative treatment for CPM patients. According to the NCCN guideline for colon cancer, patients with nonobstructing, synchronous abdominal/peritoneal metastasis are recommended to undergo systemic chemotherapy.[1] However, it also notes that "complete cytoreductive surgery and/or intraperitoneal chemotherapy can be considered in experienced centers for select patients with limited peritoneal metastases for whom R0 resection can be achieved." With less than 500 centers worldwide performing CRS and HIPEC, treatment strategies and guidelines for CPM patients differ among countries due to clinician's subjective criteria to uncontrollable factors, such as medical insurance policies. The medical system in South Korea for CPM patients is still at its early stages in incorporating CRS and HIPEC often relying on never-ending palliative chemotherapy (CTx). A recent worldwide web-based survey by the PSOGI group invited expert surgeons from 19 countries on their clinical practice regarding CRS and HIPEC in CPM patients.[2] As one might expect, the variation among countries were high.

The interest of the authors resided in the use of perioperative systemic chemotherapy. A little more than half (57.9%) supported

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https://doi.org/10.1016/j.asjsur.2023.08.135

the treatment of neoadjuvant systemic chemotherapy and 63.2% supporting adjuvant systemic chemotherapy. A systemic review by Klaver et al of 21 international guidelines regarding the treatment of CPM patients concluded that perioperative systemic chemotherapy in patients undergoing CRS and HIPEC can be considered with no consensus on duration and value.[3] Neither of the two mentioned international studies included South Korea.

There are over 115 centers in the United States dedicated to treating peritoneal carcinomatosis and 15 high volume centers performing HIPEC. More abundant number of HIPEC centers are available in Europe, and their guidelines even recommend CRS and HIPEC in CPM patients.[4] Even with this setting, the percentage of CPM patients undergoing CRS and HIPEC in the Western countries are at a mere 5–30% while majority undergo systemic chemotherapy.[5,6] The percentage is more depressing in South Korea where only 7 HIPEC centers are available and medical oncologist primarily treat CPM patients.

Ever since HIPEC was approved as a treatment option for CPM in Korea in 2013, our center performed CRS/HIPEC in highly selected patients. Due to the unique characteristics of the medical system in South Korea, we are often presented with wide range of CPM patients more often being treated with palliative systemic chemotherapy with palliative intent. We believe that carefully selected patients under palliative treatment can also benefit from CRS and HIPEC compared to systemic chemotherapy, and our unique environment allows for such comparison.

2. Materials and methods

2.1. Patient selection

Between April 2017 to October 2021, 47 patients underwent CRS. Of the 47, 31 patients underwent HIPEC by a single surgeon. The inclusion criteria for consideration of CRS and HIPEC were (1) Age 75 years or younger (2) Patients in good condition able to tolerable CRS and HIPEC (ECOG 0 or 1) (3) Pathologic diagnosis of colorectal cancer with peritoneal carcinomatosis in abdomen-pelvis computed tomography (APCT). Exclusion criteria included (1) Pathologic diagnosis of primary peritoneal cancer or low-grade mucinous neoplasm of appendix (2) Unresectable carcinomatosis of small bowel mesentery (3) Only undergoing CRS without HIPEC. Final number of 26 patients were included in the study and were analyzed. A written informed consent was not required for this retrospective study.

2.2. Surgical technique

A long midline incision was made from xiphoid process to pubic symphysis. Abdomen was opened by layer until the abdominal cavity was exposed. Omni-retractor® (Integra, Princeton, USA) was used for the exposure of all quadrants to assess peritoneal cancer index (PCI). After complete assessment of the entire abdominal cavity, proper cytoreduction was performed according to the patient's PCI. After complete cytoreduction was achieved, HIPEC was prepared. An open “Coliseum” method introduced by Sugarbaker was chosen, and the regimen used was 90 min of mitomycin C (MMC) at 25mg/BSA.[7] The temperature was set at 42 °C. Three liters of peritoneal dialysis solution was used as a carrier solution mixed with appropriately calculated MMC by patient. 50% of MMC dose was mixed initially, and each of the remaining 25% was added at 30 min and 60 min, respectively. After full 90 min of HIPEC was performed, the solution was removed completely from the abdominal cavity. Two 2-arm drains were inserted at both subdiaphragms and pelvic cavity from both sides. The abdominal fascia was closed with 1–0 STRATAFIX™ and skin with 3–0 non-absorbable monofilament (Nylon) and skin stapler. A detailed image of the CRS and HIPEC procedure undertaken by our institution is shown in Fig. 1.

2.3. Statistical analysis

All analyses were performed using R statistical Software (v4.2.1;

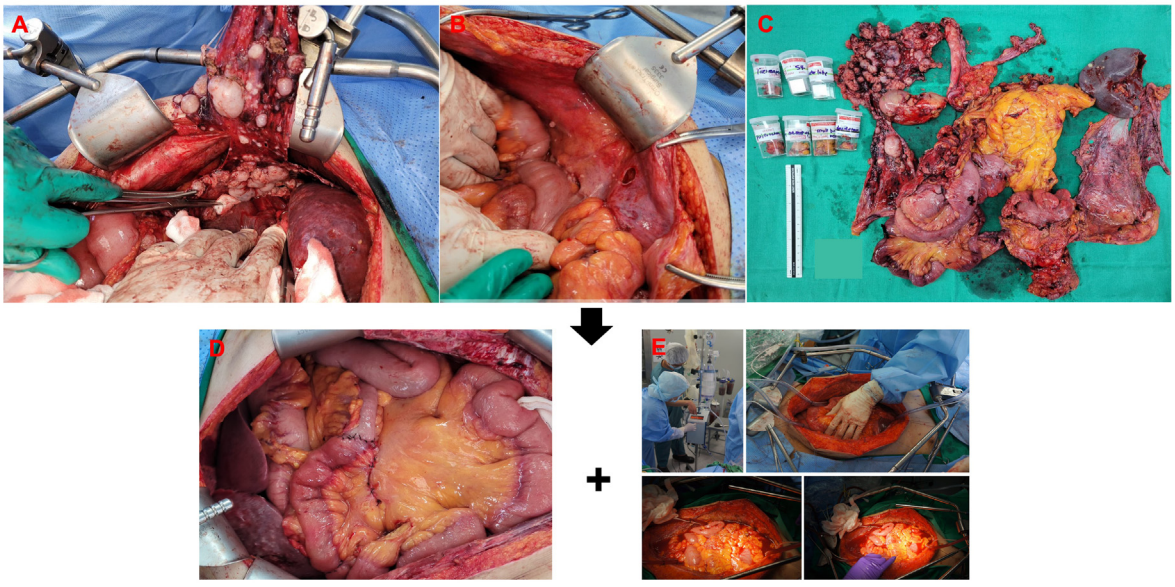

Fig. 1. Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy
A. Peritoneal metastasis
B. Pelvic peritoneum metastasis
C. Specimen after complete cytoreduction
D. After cytoreductive surgery (CCR 0)
E. Hyperthermic intraperitoneal chemotherapy in open method.

R core team 2022). *Survival* package (v3.5.0; Therneau 2023), *lubridate* package (v1.9.0; Grolemund 2011), *ggsurvfit* package (v0.2.1; Sjoberg 2022), *gtsummary* package (v1.6.3; Sjoberg 2021), and *tidycmprsk* package (v0.2.0; Sjoberg 2022) were used. Data including perioperative parameters and postoperative outcomes were analyzed.

3. Results

From April 2017 to October 2021, patients who underwent cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) were analyzed. Demographics of the patients showed 53.9% females with a median age of 56.50 years (range 14–72). Diagnosis ranged from appendiceal cancer, ascending colon cancer, descending colon cancer, rectal cancer, and sigmoid colon cancer, and the number of patients in each diagnosis is shown in Table 1. Twenty patients (76.9%) had previous operations prior to CRS and HIPEC, and the median time from diagnosis of CPM to CRS/HIPEC was 5.5 months (range 0–45). Patients were divided into two groups according to the duration of systemic chemotherapy treatment: perioperative CTx arm (≤6months) and palliative CTx arm (>6months).

The median PCI was 15.5 (range 4–39), and 96.1% of patients had complete or near complete cytoreduction (CCR0, 61.5%; CCR1, 34.6%) except for one patient with grossly remnant tumors (CCR2, 3.8%) as shown in Table 2. The mean operation time was 519.2 min (range 325–720), and eight patients received enterostomy.

The mean length of hospital stay was 15 days (range 10–39). Six patients (23.1%) had no recurrence and recurrence occurred in 20 patients (76.9%): peritoneal recurrence only (65.0%), extraperitoneal recurrence only (25.0%), and combined peritoneal and extraperitoneal recurrence (10.0%). All extraperitoneal recurrence were found in the lung. Median length of survival from initial diagnosis of colorectal cancer was 35 months (range 12–74) with median follow-up after CRS and HIPEC of 18.5months (range 4–63). At the time of this report, 18 patients (69.2%) are alive, and 8 patients (30.8%) have died. Since 69% of patients are still alive at this time, we expect our median follow-up duration to increase. The postoperative outcomes are detailed in Table 3.

Table 2
Intraoperative outcomes.

Variable	No. of patients (n = 26)
PCI	15.50 (4–39)
<10	7 (26.9%)
10-19	12 (46.2%)
≥20	7 (26.9%)
CCR	
CCR 0	16 (61.5%)
CCR 1	9 (34.6%)
CCR 2	1 (3.9%)
Operation time (min)	519.2 (325–720)
Estimated blood loss (mL)	893.8 (100–4200)
Intraoperative transfusion	
Yes	9 (34.6%)
No	17 (65.4%)
Enterostomy formation	
Yes	8 (30.8%)
No	18 (69.2%)

PCI, Peritoneal Cancer Index; CCR, Completeness of Cytoreduction.

Table 3
Postoperative outcomes.

Variable	No. of patients (n = 26)
Days to first flatus	5.8 (3–17)
Length of hospital stay	15 (10–39)
Recurrence	20 (76.9%)
Peritoneal recurrence (only)	13 (65.0%)
Peritoneal + extraperitoneal recurrence	2 (10.0%)
Extraperitoneal recurrence	5 (25.0%)
Initial diagnosis to survival (months)	35 (12–74)
Median follow-up after CRS/HIPEC (months)	18.5 (4–63)
Patient status	
Alive	18 (69.2%)
Dead	8 (30.8%)

Relapse-free survival (RFS) defined as duration from CRS and HIPEC to recurrence was 9.5 months (range 1–63) shown in Fig. 2a. Cancer-specific survival (CSS) post-CRS and HIPEC was 18.5months (range 4–63), and overall survival (OS) was 28.5months (range 9–69) shown in Figs. 2b and 3. When patients were allocated into

Table 1
Baseline characteristics.

Variable	No. of patients (n = 26)
Age (year)	56.50 (14–72)
Sex	
Male	12 (46.1%)
Female	14 (53.9%)
BMI (kg/m2)	22.97 (18.1–29.0)
ASA	
1	6
2	17
3	3
Diagnosis	
Appendiceal cancer	5
Ascending colon cancer	7
Descending colon cancer	2
Rectal cancer	3
Sigmoid colon cancer	9
Previous operation	
Yes	20 (76.9%)
No	6 (23.1%)
Treatment strategies for CPM	
CRS/HIPEC with perioperative CTx	14 (53.8%)
Palliative CTx followed by CRS/HIPEC	12 (46.2%)
Time from diagnosis of CPM to CRS/HIPEC (months)	5.50 (0–45)

CRS, Cytoreductive Surgery; HIPEC, Hyperthermic Intraperitoneal Chemotherapy; CTx, Chemotherapy; CPM, Colorectal Peritoneal Metastasis

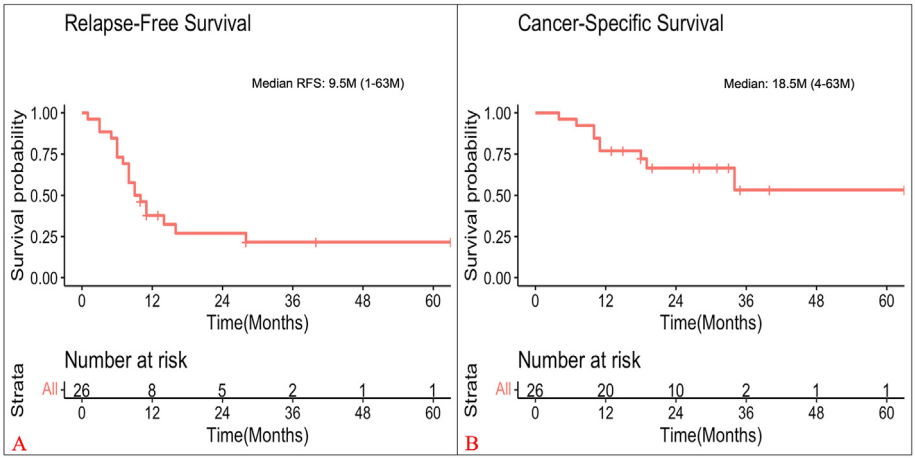

Fig. 2. Relapse free and Cancer-Specific survival after CRS/HIPEC
A. Relapse-Free Survival
B. Cancer-Specific Survival.

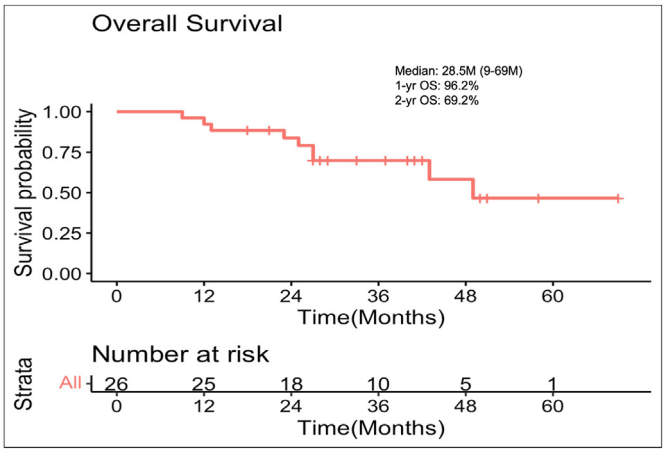

Fig. 3. Overall Survival after Initial diagnosis of CPM in CRS/HIPEC patients.

perioperative and palliative arm, the RFS increased to 13.50 months (range 3–63) in the perioperative group and reduced to 8 months (range 1–14) in the palliative group ($p = 0.014$). CSS showed the same trend with 22.50 months (range 7–63) and 16.50 months (range 4–35) in both groups, respectively with no statistical significance ($p = 0.260$). PCI score was lower in the perioperative group (13.50 vs. 15.50, $p = 0.421$). The recurrence rate was astonishing at 100% in the palliative group with only 57.1% recurrence shown in the perioperative group ($p = 0.034$). Mortality rate also doubled in the later with 41.7% compared to 21.4% in the former ($p = 0.491$). Although the survival of the patients in the two groups did not show statistically significant difference, the recur rate as well as the recurrence free survival show favorable results in the perioperative arm. With longer follow-up, we hope to see a difference in survival between the two groups. The discussed results are shown in Table 4.

There were twelve postoperative complications (46.2%) which were mostly treated with conservative care with one patient with Grade IIIb in need for re-operation (3.8%) due to small bowel perforation. There were no Grade I complications with 4 patients (15.4%) with Grade II and 7 patients (26.9%) with Grade IIIA complications. The details are shown in Table 5. When these complications were analyzed by perioperative and palliative arm, no statistically significant difference was observed (50.0% vs. 41.7%, $p = 0.976$).

Table 4
Relapse-free survival, Cancer-specific survival, and Overall survival by duration up to CRS/HIPEC after CPM diagnosis and perioperative systemic chemotherapy (months).

	Total No. of CRS/HIPEC patients (n = 26)	CRS/HIPEC with Perioperative CTx (n = 14)	Palliative CTx followed by CRS/HIPEC (n = 12)	P value
RFS (months)	9.5 (1–63)	13.50 (3–63)	8 (1–14)	0.014*
CSS after CRS/HIPEC (months)	18.5 (4–63)	22.50 (7–63)	16.50 (4–35)	0.260
OS from initial CPM diagnosis (months)	28.5 (9–69)	26 (9–69)	41.50 (21–58)	0.056
Recur rate (%, n/N)	76.9 (20/26)	57.1 (8/14)	100 (12/12)	0.034*
Mortality (%, n/N)	30.8 (8/26)	21.4 (3/14)	41.7 (5/12)	0.491
Complication (%, n/N)	46.2 (12/26)	50 (7/14)	41.7 (5/12)	0.976

	Upfront CRS/HIPEC (n = 6)	CRS/HIPEC after 1st line CTx (n = 12)	CRS/HIPEC after 2nd or more line CTx (n = 8)	P value
RFS (months)	22 (6–40)	10 (3–63)	7.50 (1–14)	0.145
CSS after CRS/HIPEC (months)	26.50 (11–40)	16.50 (8–63)	18.50 (4–34)	0.614
OS from initial CPM diagnosis (months)	26.50 (12–40)	29 (9–69)	41.50 (25–51)	0.292
Recur rate (%, n/N)	50 (3/6)	75 (9/12)	100 (8/8)	0.087
Mortality (%, n/N)	16.7 (1/6)	25 (3/12)	50 (4/8)	0.344
Complication (%, n/N)	50 (3/6)	33.3 (4/12)	62.5 (5/8)	0.430

CRS/HIPEC, cytoreductive surgery and hyperthermic intraperitoneal chemotherapy; CPM, colorectal peritoneal metastasis; RFS, relapse free survival; CSS, cancer-specific survival; OS, overall survival; CTx, chemotherapy.
*$p < 0.05$ showing statistical significance.

Table 5
Complications according to Clavien-Dindo classification.

Variable	No. of patients (n = 26)
Postoperative complication	
No	14 (53.8%)
Yes	12 (46.2%)
Grade I	0 (0%)
Grade II	4 (15.4%)
Ileus	3
Pseudomembranous colitis	1
Grade IIIA	7 (26.9%)
Pleural effusion	6
Intraabdominal infection	1
Grade IIIb	1 (3.8%)
Small bowel perforation	1

4. Discussion

Peritoneal metastasis is the third most common organ of metastasis next to liver and lung, accounting for 11% of CRC patients.[8] Once believed to be a systemic disease, some surgical oncologists now believe it to be a loco-regional disease warranting loco-regional treatment with emerging ideas that surgical approach to CPM patients may be a treatment option given the poor prognosis with IV therapeutics.

In 1996, a French group of colorectal surgeons led by Elias initiated a trial with a working hypothesis that a previous 2-year survival rate of 10% could be increased to 40% with complete cytoreduction followed by early postoperative intraperitoneal chemotherapy (EPIC).[9] After undergoing cytoreductive surgery, patients were randomized to a control group of systemic chemotherapy (5-fluorouracil, 5-FU) and an experimental group of EPIC (mitomycin C). The results were shocking to the medical community as both groups showed unexpectedly high overall survival rate of 60% at 2 years, compared to the previously known 10% when treated only with systemic chemotherapy. Although deemed as a failed trial with early termination due to failed patient recruitment, Elias' trial provided a stepping stone for the efficacy and benefits of cytoreductive surgery in CPM patients.

Since the first randomized controlled trial (RCT) regarding the effect of CRS and HIPEC versus systemic chemotherapy with 5-FU and leucovorin demonstrated favorable oncologic outcomes in the former (disease specific survival rate 22.2 months vs 12.6 months), HIPEC centers around the world have supported this procedure as one of the treatment strategies in CPM.[10] An 8-year follow-up of the patients showed a median progression-free survival of 7.7 months in the standard group compared to 12.6 months in the CRS and HIPEC group ($P = 0.032$).[11] In an updated non-randomized study by Franko et al using modern chemotherapy, the duration of survival measured from CPM diagnosis was prolonged to 16.8 months.[12] When CRS and HIPEC were performed, the duration doubled to 34.7 months ($P < 0.001$) and even as high as 62.7 months ($P < 0.05$) in one group.[13]

Medical system in South Korea relies heavily on the policies and regulations set by the Ministry of Health. Approved in July 2013, CRS and HIPEC have been performed by only a handful number of surgeons in the country interested in this field of peritoneal metastasis. Over the past decade, colorectal surgeons have increased the awareness of CRS and HIPEC in CPM; yet the number of centers at which HIPEC is available is at its mere seven centers. Majority of CPM patients are treated by medical oncologists skeptical of the effect of CRS and HIPEC, thus relying heavily on palliative systemic chemotherapy and therapeutic agents. Under such system, CPM patients in South Korea have a different treatment course from those in Europe and United States where CRS and HIPEC is more accessible. Comparing the data between these two groups would be difficult and imprecise.

Studies regarding CRS and HIPEC enroll patients in neoadjuvant or adjuvant setting and often designate a systemic chemotherapy-free period prior to enrollment.[6,11,13] However, in South Korea, CPM patients are almost always being treated with systemic chemotherapy. Therefore, we the authors pondered whether CRS and HIPEC was beneficial in improving OS and RFS in this palliative setting.

CAIRO6 study assessing the value of perioperative systemic therapy prior to CRS and HIPEC mentions benefits and risks of perioperative systemic therapy.[6] In a neoadjuvant setting, systemic chemotherapy can decrease tumor burden prior to surgery in resulting of more complete cytoreduction. More importantly, however, it can help select patients who would most benefit from CRS and HIPEC agreed by most experts in the field.[2] The drawbacks are not insignificant as intravenous systemic chemotherapy is known to be impermeable in peritoneal carcinomatosis and may lead to disease progression in some patients.[14] In that effect, patients may become ineligible for CRS and HIPEC due to disease progression. There are a few retrospective reviews on the role of neoadjuvant chemotherapy in CPM settings.[15–17] Chen et al discussed the result of neoadjuvant chemotherapy in appendiceal cancer patients.[16] In a propensity-score matched analysis of patients who received neoadjuvant chemotherapy (NC) and patients with upfront surgery, the former showed worse overall survival and relapse-free survival than the later. The results coincide with previous reports of worse prognosis with NC.[18–21] Beal et al also reviewed the impact of NC undergoing CRS with or without HIPEC and found no benefit in improving OS or RFS.[15] There are, of course, studies with conflicting results.[22–24] The NC regimen used, the addition of target agents, and the duration of the NC vary between studies yielding conflicting results with no concrete consensus. Patient factors and histopathologic factors can be biased in the NC group forbidding proper comparison.

Adjuvant systemic chemotherapy after CRS and HIPEC is more accepted than neoadjuvant therapy.[3] Postoperative eradication of both intraperitoneal and systemic microscopic tumor is the utmost advantage of systemic therapy in adjuvant setting leading to longer PFS and OS.

Waite et al reviewed 14 studies that discussed the use of adjuvant chemotherapy.[17] Overall, numerous studies showed improved OS of 8–10 months with adjuvant chemotherapy.[22,25–28] However, the duration, the regimen, and the timing of the adjuvant chemotherapy administered vary among studies to form a consensus.

In our study, 20 patients (76.9%) received previous operation for the main tumor lesion prior to visiting our center for CRS and HIPEC all of whom underwent adjuvant chemotherapy after initial surgery. Six patients without previous surgery were patients diagnosed with CPM at initial diagnosis of primary colorectal cancer and were treated with upfront CRS and HIPEC without neoadjuvant chemotherapy. Based on our data, the treatment strategy of CRS and HIPEC with perioperative CTx seemed to be more beneficial than that of CRS/HIPEC after longer duration of systemic CTx (RFS 13.5 vs. 8; CSS 22.5 vs. 16.5). We believe that the longer the follow-up duration, the difference in recur rate (57.1% vs. 100%) and mortality rate (21.4% vs. 41.7%) between perioperative and palliative arm will become more apparent. As shown in Table 4, one patient in perioperative arm was diagnosed with complete remission, and one patient with no evidence of recurrence at 40 months will soon undergo complete remission as well. As evidence show all patients in the palliative arm have recurred, early CRS and HIPEC in selective patients may be the only curative option for complete remission.

In a subgroup analysis, the authors divided the patients into three groups: (1) Upfront CRS/HIPEC (2) CRS/HIPEC after 1st line

systemic chemotherapy (3) CRS/HIPEC after 2nd or more line systemic chemotherapy shown in Table 4. RFS of the upfront group was 22 months (range 6–40) compared to 10 months (range 3–63) in 1st line group and 7.50 months (range 1–14) in 2nd or more line group ($p = 0.145$). We can infer from the results that patients requiring advanced line systemic therapy may have tumors with poor characteristic and behavior showing resistance to the systemic therapy itself as well as rapid progression of the disease. The recurrence rate doubles to 100% in patients undergoing chemotherapeutic agents in 2nd line or more. Mortality also shows an upward trend of 16.7%, 25%, and 50% in each group, respectively, but was not statistically significant ($p = 0.344$).

In determining the course of a patient's treatment, factors such as histology, PCI, attainability of CCR 0–1 are considered. In synchronous CPM patients with favorable histology and PCI of less than 15 with high likelihood of complete cytoreduction, upfront surgery is considered. However, in unfavorable pathology such as signet ring cell with PCI score of more than 15, neoadjuvant CTx is offered with periodic follow-up of the status of the disease to determine the eligibility of CRS/HIPEC.

The general atmosphere of the medical oncologists needs a shift from relying only on systemic chemotherapy to opening treatment options to CRS and HIPEC. The importance of multidisciplinary approach to a patient's care is being emphasized in all fields of medicine, especially in oncology. Patients diagnosed with CPM should be referred to expert CRS/HIPEC centers, and through multidisciplinary team including surgical oncologists, medical oncologists, as well as radiologist, appropriate patient selection for CRS/HIPEC should be made.

Moreover, there is a limitation of current radiologic studies in diagnosing small peritoneal metastasis, especially along small bowel mesentery leading to lower CT-PCI score compared to intraoperative PCI score. For this reason, our current practice advises patients with CT-PCI of 15 or more to undergo neoadjuvant chemotherapy prior to CRS/HIPEC. Patients with ECOG 0–1, less than 75 years of age, PCI <20, and possible CCR 0–1 are cut-offs for CRS/HIPEC.

Survival measured from CPM diagnosis in patients treated with modern systemic chemotherapy is 16.8 months.[12] The overall survival of all patients in our study was 28.5 months (range 9–69). In subgroup analysis by levels of chemotherapy, upfront group showed OS of 26.50 months (range 12–40) compared to 29 months (range 9–69) in 1st line group and 41.50 months (range 25–51) in 2nd or more line group ($p = 0.292$). Although the increased duration is mainly due to the prolonged period of palliative chemotherapy, it shows that patients even under palliative setting in whom CRS and HIPEC were performed can improve survival compared to the known 16.8 months after systemic chemotherapy only. Nonetheless, the earlier the CRS and HIPEC was performed, the better the outcome in RFS and CSS after CRS and HIPEC. As multidisplinary therapy is recommended in the treatment of stage IV colorectal cancer in almost all guidelines, medical oncologists and surgical oncologists should discuss the course of the treatment together to propose the best course of treatment for CPM patients.

The most recent update to CRS and HIPEC was the PRODIGE 7 trial conducted by Quenet et al.[29] PRODIGE 7 study was a randomized, open-label, phase 3 multicenter trial which compared cytoreductive surgery with or without oxaliplatin-based HIPEC among patients diagnosed with peritoneal carcinomatosis originating from colorectal cancer. This study concluded that there was benefit of CRS but the addition of HIPEC did not show overall survival benefit of HIPEC to cytoreductive surgery alone (OS 41.7 months vs 41.2 months, RFS 13.1 months vs 11.1 months), but rather increased 60-day complications in the HIPEC group. Although uptodate studies regarding HIPEC have not yet announced favorable outcome, CRS has proven its benefit.[9,11]

After the announcement of the preliminary results of PRODIGE 7 study in ASCO 2018, experts around the world have modified their treatment strategy regarding the regimen and the duration of HIPEC to Mitomycin C and 60–90 min.[30] Mitomycin C version of PRODIGE 7 trial known as GECOP-MMC (NCT05250648) is ongoing as well as HIPECT 4 trial evaluating MMC-based HIPEC as adjuvant therapy is awaiting results.[31,32]

There are couple of limitations with our study. A retrospective design often accompanies selection bias. Five appendiceal cancer patients were included in our study, and the different prognosis of appendiceal cancer and colorectal cancer may have affected the results. Due to the low number of patients exposed to CRS and HIPEC in South Korea, a small sample size is also a drawback. Our center, although retrospectively reviewed with a small sample size, used MMC-based HIPEC regimen for 90 min as well and will continue to do so hopeful that GECOP-MMC and HIPECT4 will bring positive results of HIPEC.

5. Conclusion

CRS and HIPEC could be a treatment option for a carefully selected CPM patients. Although the short median follow-up in the perioperative CTx group hinders proper comparison of overall survival between the two groups, overall survival of 41.50 months (range 21–58) in palliative group compared to 16.8 months from the literature undergoing systemic CTx only supports CRS and HIPEC even in palliative patients. Although the percentage of postoperative complications were high at 46%, they were manageable and were discharged without any sequelae affirming that CRS and HIPEC can be safely performed in experienced surgeons.

Statement of ethics

This study was approved by the Institutional Review Board and Ethics Committees of Bundang CHA Medical Centre (IRB No:2022-11-006) and was conducted according to the principles of the Declaration of Helsinki. A written informed consent was not required for this retrospective study.

Funding sources

None.

Author contributions

Conception and design of the study: Woo Ram Kim, Jong Woo Kim, Hye Jung Cho; data acquisition: Woo Ram Kim, Hye Jung Cho; statistical analysis: Woo Ram Kim, Hye Jung Cho; supervision or mentorship: Woo Ram Kim, Jong Woo Kim. Each author contributed to the article and approved the submitted version.

Data availability statement

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of competing interest

The authors state that there is no conflict of interest.

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