Outcomes of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in the treatment of primary peritoneal carcinoma

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Abstract

Primary peritoneal carcinoma (PPC) is rare tumor, traditionally treated with surgical debulking and systemic chemotherapy (SC) with 30% five-year survival rate. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) may improve long-term survival.

Thirty patients with PPC were identified. Twenty-three patients underwent CRS/HIPEC as initial treatment (group I) and 7 for recurrent disease (group II). Peritoneal cancer index (PCI), cytoreduction scores (CC), overall survival (OS) and progression-free survival (PFS) were estimated using Kaplan-Meier survival analysis.

FIGO stages II/III/IV at diagnosis were 2/20/7 (1 was not classified). Median time from diagnosis to CRS/HIPEC was 2 months and 8 months in groups I and II, respectively. PCI≥20 was seen in 16 (70%) and 4 (57%) in groups I and II, respectively. Complete cytoreduction (CC 0-1) was achieved in 30/32 (94%) CRS/HIPEC procedures. Median follow-up was 39 months (range: 11-250). PFS at 1, 3, 5-years was 80%, 75%, 59%, respectively. OS 1, 3, 5-years from CRS/HIPEC was 90%, 68%, 55%.

CRS/HIPEC and adjuvant SC provides five-year survival rate higher than previously reported for PPC patients who received conventional therapy with surgical debulking and SC.

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Key words: Primary peritoneal carcinoma; cytoreductive surgery; HIPEC; outcomes.

Acknowledgments: the authors would like to thank Ryan MacDonald, PhD for providing the statistical and data analysis, and Roy Hatch for literature search.

Contributions: AS1, AS2, VG, study concepts; AS1, study design; AS2, MS, data acquisition; AS1, AS2, MS, quality control of data and algorithms; AS1, AS2, VG, KS, data analysis and interpretation; RMD, AS2, statistical analysis; AS2, MS, CN, manuscript preparation; AS1, AS2, MS, CN, VG, manuscript editing; AS1, AS2, VG, manuscript review.

Conflict of interest: all authors declare no conflict of interest.

Received for publication: 9 February 2017.
Revision received: 12 June 2017.
Accepted for publication: 15 June 2017.

Journal of Peritoneum (and other serosal surfaces) 2017; 2:57
doi:10.4081/joper.2017.57

Introduction

Primary peritoneal carcinoma (PPC) is thought to account for 10% of ovarian malignancies[1] and is most often diagnosed during the 6th decade of life as an ovarian/extra-ovarian malignancy, a Mullerian tract origin malignancy, or carcinoma of unknown primary. Approximately, 15% of ovarian surface malignancies actually have a primary peritoneal origin,[2] with similarities including common embryologic origin, identical immunohistophenotype characteristics,[3,4] and similar germline mutations (BRCA1, BRCA2),[5] which have resulted in similar treatment approaches for both diseases.[6,7] However, recent histopathological evidence suggests that PPC may originate from multiple individual sites in the peritoneal cavity as opposed to the singular clonal origin of ovarian cancer (OC).[8,9]

Conventionally, patients presenting with PPC or ovarian cancer, have been treated with cytoreductive surgery (CRS) and systemic chemotherapy (SC). However, tumor progression rates remain high. We reviewed the outcomes of PPC patients presenting with or without prior surgical and/or systemic treatment, who subsequently underwent CRS/HIPEC.

Materials and Methods

A retrospective review of 30 PPC patients who underwent CRS/HIPEC from October 1994- September 2015 was carried out. The diagnosis of PPC was based on clinical and histopathological findings established by the Gynecologic Oncology Group and described by Bloss *et al.*:[10] i) ovaries normal in size, enlarged due to the benign process, or absent; ii) involvement of the extra-ovarian sites of peritoneal surface greater than in either ovary; iii) absent or limited involvement of ovarian surface or cortical stroma with the nodule not exceeding 5x5 mm; iv) histopathology and

cytology characteristic predominantly serous or similar to ovarian serous papillary adenocarcinoma of any grade. The WHO classification for tumors of female reproductive organs and recommendations of international collaboration on cancer reporting (ICCR) was also used for histological classification.[11]

Patient evaluation and treatment

Radiographic imaging (CT scan of the chest, abdomen, and pelvis) and tumor markers (CEA, CA19-9, and CA 125) were obtained prior to surgery. Tumor markers were considered positive if CEA was ≥5 ng per mL, CA 19-9 ≥37 units per mL, CA 125 ≥35 units per mL.[12] Surgery was recommended if complete cytoreduction (CC) was deemed feasible by the operating surgeon. Complete cytoreduction was defined as residual nodules less than 2.5 mm in size (CC=1) or the absence of any visible tumor nodules (CC=0).[13]

The Peritoneal Cancer Index (PCI), as previously described by Jacquet et al., was used to assess the extent of peritoneal involvement.[13] When available, histopathology from CRS/HIPEC, as well as the first surgery or biopsy was reviewed at our institution. Lymph node (LN) status was obtained from the pathology report.

Definitive CRS was carried out to achieve complete cytoreduction (CC) using, but not limited to, the following procedures: exploratory laparotomy, umbilectomy, abdominal and pelvic lymphadenectomy, appendectomy, cholecystectomy, cytoreductive surgery, biopsy of peritoneal implants, enterolysis, ureterolysis, and partial vaginectomy. The peritonectomy procedures include but were not limited to diaphragmatic, parietal and pelvic peritonectomy, and omentectomy. Organ resection was performed when it was not possible to completely cytoreduce the surface of the organ. Every effort was made to avoid extensive small bowel resection and/or ostomy formation to help maintain quality of life.

The HIPEC procedure was performed immediately following cytoreduction, of which details have been previously reported.[14] Chemotherapeutic agents used included cisplatin (50 mg/m^2) with doxorubicin (15 mg/m^2), mitomycin-C (30 mg initially plus 10 mg added 30 minutes later), carboplatin (800 mg/m^2), melphalan (50 mg/m^2), mitomycin-C with doxorubicin (40 mg/m^2), and 5-FU with mitomycin-C (dosage not documented). The chemotherapeutic perfusion agent used in each case was based upon previous drug resistance assay and history of relapse with platinum agents. Melphalan was used in cases of known platinum resistance. The duration of each perfusion was 90 minutes using the closed technique.

Dosages of chemotherapeutic agents were determined empirically, based on their use in HIPEC from diagnoses other than PPC (*i.e.*, ovarian, appendiceal, colon), and results of tumor resistance panels.

Statistical analysis

Clinical data was prospectively collected at the time of follow-up visits. Statistical analysis was performed using the SPSS 23.0 statistical software package (IBM Corp., Armonk, NY USA). Median follow-up and overall survival were calculated from the date of surgery until death, or last follow-up visit. Estimation of survival was calculated using the Kaplan-Meier method with log-rank test to compare survival rates. Progression-free survival (PFS) was defined as no evidence of disease by physical exam, CT scan, and/or normal tumor markers and was calculated from the date of CRS/HIPEC to date of recurrence, or date of last encounter. Deaths were not assumed as an event. PFS was only estimated for patients with complete cytoreduction. Postoperative deaths were included in survival analysis. Cox proportional hazard ratio was used to evaluate the role of lymph node (LN) status, PCI score, and CC score in terms of overall survival (OS). Results were considered statistically significant if P≤0.05.

Patients with 2 HIPEC procedures were included in survival analysis from the time of first CRS/HIPEC until last follow-up/date of death. These patients were only included in the PFS analysis once; time from the first CRS/HIPEC procedure until the time of the first recurrence. The second recurrence was not included in the PFS analysis.

Study endpoints

The primary endpoint of our study was to determine the overall and progression free survival in patients with PPC. The secondary endpoint evaluated the prognostic criteria for survival in patients with PPC.

Patient assignment

Patients were subdivided into groups based on initial and recurrent therapy. The initial group (n=23) included patients who received CRS/HIPEC as an initial treatment or who received neo-adjuvant chemotherapy (NACT) without prior surgical resection. The recurrent group (n=7) included patients who underwent previous surgical treatment before CRS/HIPEC.

Results

Patient characteristics

Thirty patients with PPC treated with CRS/HIPEC were included in the study. Clinicopathological characteristics are listed in Table 1. Median age at the time of CRS/HIPEC was 60 years (range: 40-75). Twenty-four (80%) women were diagnosed with high-grade peritoneal serous carcinoma (HGPSC), 3 (10%) low-grade peritoneal serous carcinoma (LGPSC), 1 (3%) clear cell carcinoma, 1 (3%) mucinous carcinoma, and 1 (3%) was not classified. FIGO staging at initial diagnosis was reviewed with the majority of patients (90%) presenting with advanced disease: 2 stage II (7%), 20 stage III (67%), and 7 stage IV (23%). Staging was not available for one patient.

Chemotherapy and CRS/HIPEC

A total of 32 HIPEC procedures were performed on 30 patients, including 2 patients who received two CRS/HIPEC procedures secondary to tumor recurrence. Specific chemotherapy agents used in HIPEC are listed in Table 2.

Median PCI was 29 (range: 4-39). Of the 30 patients, 20 (66.7%) had PCI scores ≥20: 16 (70%) in the initial treatment group and 4 (57%) recurrent patients. A complete cytoreduction (CC-0/CC-1) was achieved in 30/32 (94%) CRS/HIPEC procedures. Two patients had incomplete cytoreduction (CC-2) after CRS/HIPEC with pre-operative PCI scores of 34 and 39.

Median length of surgery was 9 hours and did not vary significantly among groups. In 32 CRS/HIPEC procedures, overall grade III-V complications were seen in nine patients (28%), 8/23 (35%) in the initial group, and 1/7 (14%) in the recurrent group, as classified by the Clavien-Dindo surgical classification system.[15] Overall median hospital stay was 12 days. There were two cases of hospital mortality and one thirty-day perioperative death, which occurred after hospital discharge from unknown causes. The two cases of hospital mortality included a 71-year-old with a gastric fistula who died 45 days postoperatively from sepsis, and a 72-year-old who died 29 days postoperatively from *Clostridium difficile* sepsis and respiratory failure.

Twenty-five patients (83%) received adjuvant combined systemic taxane/platinum based chemotherapy regimens. Five

patients did not undergo adjuvant chemotherapy: 2 patients had low grade tumors which chemotherapy was not indicated and 3 others, due to mortality. One patient with a history of lymphoma, had a lymphoma recurrence and was treated with bendamustine and rituximab. Two patients underwent repeated CRS/HIPEC procedures after tumor progression. The first patient initially received NACT (carboplatin/paclitaxel, x10 cycles) for extensive disease, followed by CRS/HIPEC with mitomycin-C (PCI 31/0, CC-0) plus adjuvant chemotherapy (docetaxel). Intraperitoneal recurrence was detected 9 months after the first CRS/HIPEC. A repeat CRS/HIPEC was performed 13 months after the first procedure (PCI 5/0, CC-0) and the patient died 11 months later, 25 months after initial HIPEC. The other patient, initially treated with CRS/HIPEC (doxorubicin/mitomycin-C) for extensive disease (PCI 34/0, CC-1) plus adjuvant chemotherapy (carboplatin/paclitaxel), had intra-peritoneal recurrence 63 months later. One month after recurrence, she underwent a repeat CRS/HIPEC with melphalan (PCI 8/0, CC-0). The patient remains NED 68 months after the second procedure with 133 month overall survival since the first CRS/HIPEC.

Survival and prognostic analysis

Median follow-up was 39 months (range 11-250 months). Median time from diagnosis to CRS/HIPEC was 2 months (range: 0-37) for all patients, <2 months (range: 0-9) for initial group, 5 months (range: 3-9) for NACT patients, and <1 month without NACT (range: 0-2). Median time to diagnosis and CRS/HIPEC in the recurrent group was 8 months (range: 2-37).

Seventeen patients had at least one positive preoperative tumor marker (CA-125, CA-19-9). CEA was found to be within normal range in all patients. Tumor markers failed to show prognostic significance. Seventeen patients (56.7%) are alive: 15 (50%) without evidence of disease and 2 (6.7%) alive with disease. Twelve disease-related deaths occurred (40%). One patient died 21 years after CRS/HIPEC, due to liver failure, with no evidence of recurrent disease.

Table 1. Clinicopathologic characteristics.

Variable	All patients (n=30)	Initial (n=23)	Recurrent (n=7)
Median age at the time of diagnosis, years (range)	60 (40-73)	60 (44-73)	52 (40-71)
Median age at the time of CSR/HIPEC, years (range)	60 (40-75)	60 (44-75)	54 (40-75)
Histological subtype, n (%)			
HGPSC	24 (80)	19 (83)	5 (71)
LGPSC	3 (10)	2 (9)	1 (14)
Clear cell carcinoma	1 (3)	1 (4)	-
Mucinous carcinoma	1 (3)	1 (4)	-
Unknown	1 (3)	1 (4)	-
FIGO staging			
Stage II	2 (7)	1 (4)	1 (14)
Stage III	20 (67)	16 (70)	4 (57)
Stage IV	7 (23)	6 (26)	1 (14)
Unidentified	1 (3)	-	1 (14)
Status, n (%)			
Alive	*17 (57)*	*12 (52)*	*5 (71)*
NED	15 (50)	12 (52)	3 (43)
WD	2 (7)	-	2 (29)
Deceased	*13 (43)*	*11 (48)*	*2 (29)*
DOD	12 (40)	11 (48)	1 (14)
DOC	1 (3)	-	1 (14)
Median time from diagnosis to CRS/HIPEC, months (range)	2 (0-37)	2 (1-9)	10 (2-37)
Median follow-up time from CRS/HIPEC, months [IQR]	39 [19-60]	29 [19-55]	41 [29-92]
CRS/HIPEC procedures	32	25	7
PCI Score ≥20, n (%)	20 (67)	16 (70)	4 (57)
CC 0-1, n (%)	30 (94)*	23 (92)°	7 (100)
LN Status positive, n (%)	17 (57)	13 (43)	4 (57)
Median length of surgery, minutes	541	543	579
Median hospital stay, days	12	14	12
Post-operative complications grade III/IV/V (Clavien-Dindo) (%)°	9 (28)	8 (32)	1 (14)
30-day mortality, n (%)	2 (7)#	2 (8)	-
Alive	*17 (57)*	*12 (52)*	*5 (71)*
NED	15 (50)	12 (52)	3 (43)
AWD	2 (6.7)	-	2 (29)
Deceased	*13 (43)*	*11 (48)*	*2 (29)*
DOD	12 (40)	11 (48)	1 (14)
DOC	1 (3)	-	1 (14)

HGPSC, high-grade serous carcinoma; LGPSC, low-grade serous carcinoma; IQR, interquartile range; NED, no evidence of disease; AWD, alive with disease; DOC, dead of other causes; DOD, dead of disease; CC, completeness of cytoreduction; LN, lymph node; PCI, peritoneal carcinomatosis index; *calculated from 32 CRS/HIPEC procedures; °total 25 CRS/HIPEC procedures in this group; #one patient died of sepsis, other due to respiratory failure.

Median overall survival (n=30) was 68 months (95% CI: 0-149). The 1, 3, and 5-year overall survival since diagnosis was 90%, 68%, and 55%, respectively. The median survival in the initial group was 56 months (95% CI: 28-85 months), while median survival in recurrent patients was not reached. Overall survival in the initial group at 1, 3, and 5-years was 87%, 63% and 46%, and 100%, 83%, and 83% in the recurrent group (P≤0.2) (Figure 1).

PFS was estimated for patients with complete cytoreduction (n=28). Median PFS in all patients was 62 months (95% CI: 43-82 months) with 1, 3, and 5-years disease free survival of 80%, 75%, and 59%, respectively. Both groups reached a median DFS of 63 months (95% CI: 34-93 months) in the initial group and (95% CI: 34-91) in the recurrent group. PFS at 1, 3, and 5-years was 78%, 71%, and 59% for initial patients, and 86%, 86%, and 57% for patients treated after recurrence (P≤1) (Figure 2).

Univariate analysis showed PCI score to be the only statistically significant prognostic factor of OS (HR 1.13; 95% CI: 1.02-1.25) (P<0.02), while LN status and CC scores failed to show any statistically significant impact.

Multivariate analysis failed to identify prognostic factors

Patients without treatment prior to CRS/HIPEC had no survival benefit compared to patients treated with debulking surgery and/or SC before HIPEC.

Discussion

There are few published studies on primary peritoneal carcinoma. The majority of these studies incorporate PPC within ovarian cancer. Studies of OC with CRS/HIPEC have shown vast median survival ranges of 22-66 months in patients with peritoneal carcinomatosis of ovarian origin.[16-18] Patients with PPC are often included in the OC patient population, which could mask survival results making it difficult to conclude the natural history of disease. Recent studies have found differences in biologic, histopathologic, genetic, and clinical behavior of these diseases.[2,6,8,9,19,20] The role of CRS/HIPEC was evaluated in patients with a strict diagnosis of PPC, excluding ovarian histopathology.

Conventional therapy for patients with PPC is surgical debulking followed by systemic chemotherapy; however, survival outcomes remain poor. Kawaguchi *et al.* compared treatment outcomes of 22 PPC patients with 55 advanced OC patients and obtained lower median PFS (12.7 months, 95% CI: 6.3-19.1) and OS (26.5 months, 95% CI: 14.7-38.3) in PPC compared to OC (PFS: 15.9 months and OS: 38.8 months).[19] Improved survival was achieved in a study by Eisenhauer *et al.*,[6] with median OS of 42 months for PPC patients, however, these findings suggest the necessity for other treatment modalities in patients with PPC.

Cytoreductive surgery is a relatively recent and technically demanding procedure in surgical oncology. The quality of the surgery and its philosophy has evolved significantly over the last 3 decades. Surgeons have to acquire considerable expertise that comes with the great number of surgical procedures performed during the careers. At our high-volume peritoneal malignancy center, two surgical oncologists have performed a total of 613 CRS/HIPEC procedures from 1994 to 2015. In this cohort of PPC patients (n=30); one surgeon performed 29 procedures in 27 of these patients and the other surgeon performed the remaining 3. Despite the small number of HIPEC procedures performed in PPC, the same complex surgical techniques for appendiceal, colon, recurrent ovarian cancers, and malignant mesothelioma with peritoneal dissemination were applied, which requires multiple organ resections in order to obtain a complete cytoreduction. Over time, our experience has allowed us to obtain the necessary and valuable knowledge to achieve optimal cytoreduction despite the complexity of these cases.

Data specific to the role of HIPEC for PPC is very limited. Survival in patients with PPC treated with CRS/HIPEC reported in

Table 2. HIPEC perfusion agents.

Chemotherapy agent	Number of HIPEC proce-
Carboplatin	13
Mitomycin-C	6 (1)*
Doxorubicin/cisplatin	5
Melphalan	4 (1)°
Mitomycin/doxorubicin	1
5-FU/mitomycin-C	1

*Repeated in 1 patient after recurrence; °used after recurrence in patient previously received mitomycin-C/doxorubicin.

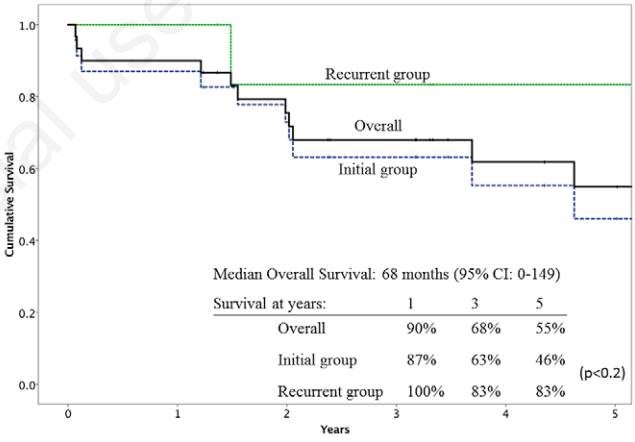

Figure 1. Survival since CRS/HIPEC.

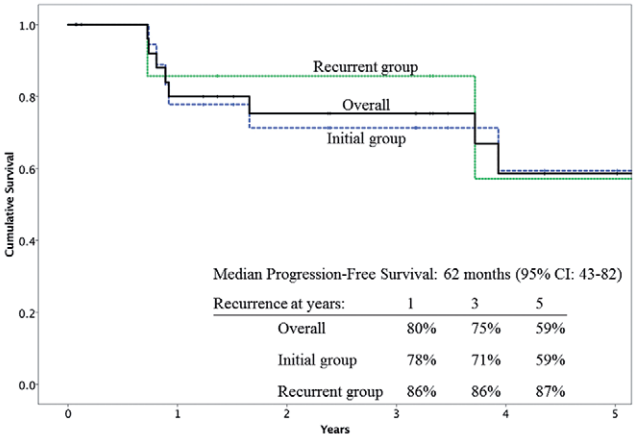

Figure 2. Progression-free survival since CRS/HIPEC.

other studies is summarized in Table 3. In a retrospective multicenter study by Bakrin *et al*., 36 PPC patients treated with CRS/HIPEC had mortality and morbidity rates of 5.6% and 20.6%, respectively. The overall 1, 3, and 5-year survival was 93.6, 71.5, and 57.4%.[21] These results are similar to our study (90%, 68%, and 55%, respectively), however, we did not exclude mortality from survival analysis. Our data also confirmed the findings of Bakrin *et al*., supporting PCI scores as the only prognostic hazard factor.[21] It is encouraging that both studies, conducted at different institutions and different continents, led to similar results. Our data supports the conclusion of Barkin et al., that CRS/HIPEC may achieve better long-term survival than the current treatment modalities. We found that patients who presented after previous treatment had an improved 5-year survival rate of 86%, although this was not statistically significant. This might be explained by careful patient selection or by the small cohort (n=7) of patients. Also, in our study, patients who initially presented with more advanced disease underwent neo-adjuvant chemotherapy delaying time to CRS/HIPEC. This may bias the initial group to poorer outcomes when compared to patients who present after relapse, since 4 of the 6 patients who underwent NACT have died of disease. The rarity of this type of surface peritoneal carcinomatosis explains the small cohort, while a larger cohort could provide a better basis of comparison.

In this study, PFS at 3- and 5-years was greater than OS because 2 patients with incomplete cytoreduction (CC-2) were excluded from the analysis. Therefore, the time to recurrence was extended in the PFS analysis.

Our study is quite similar to a recent study by Sun *et al*.[22] who compared two groups of PPC patients: advanced PPC without prior surgical treatment (n=12), to recurrent PPC patients (n=10) with heterogenous treatment regimens. Sun *et al.* achieved complete cytoreduction (CC 0-1) in 68% with reported OS of 100%, 45.5% and 27.3% at 1, 3, and 5-years, respectively. They also found PCI to be the only prognostic factor however, we used PCI score ≥20, while they used PCI ≤15. In our study, CC 0-1 was achieved in 93% of patients, which suggests the importance of complete surgical removal of all visible tumor for improved long term survival, explaining our higher survival rates.

The most effective intraperitoneal chemotherapy regimen for PPC or ovarian cancer has not been clearly defined. The efficacy of intravenous platinum agents as systemic therapy for ovarian cancer is well known, therefore, these agents have also been used as perfusion agents in HIPEC for ovarian cancer, with a similar pharmacokinetic advantage.[23] However, Eisenhauer et al. found a higher rate of resistance to platinum-based chemotherapy in patients with PPC compared to OC.[6] Thus, we used platinum-based agents for CRS/HIPEC procedures as a first line treatment, but preferred melphalan for PPC patients who have failed previous conventional therapy.

Regardless of histology, mitomycin-C was the primary agent of choice for HIPEC perfusion, and also used in PPC.[21,22] The effects and mechanisms of hyperthermia have become clearer and mitomycin-C was replaced by platinum-based agents. The Gynecologic Oncology Group (GOG) supported the role of IP cisplatin in ovarian patients as the ideal chemotherapy treatment following surgical debulking.[23] Therefore, in 2006, we used either a single-based platinum agent or combination platinum-based agent with doxorubicin; replacing mitomycin-C. Additionally, our decisions were guided by chemotherapy sensitivity and resistance assays. Dosages of these drugs were determined empirically, and were within known therapeutic range.

Based on our experience,[14] melphalan has been shown as an efficacious alternative in patients undergoing HIPEC for recurrent peritoneal surface malignancies. It has also been reported that melphalan enhances cytotoxicity under hyperthermic conditions, due to better drug penetration.[24] Additionally, our decision to use melphalan in recurrent cases was based on data reporting the benefit of melphalan in recurrent platinum- and taxane-resistant ovarian cancer[25] and the successful use of melphalan in aggressive resistant neoplasms (soft tissue sarcoma).[26]

Our improved long-term survival results could also be

Table 3. Treatment regimens and survival in patients with primary peritoneal carcinoma treated with CRS/HIPEC reported by study.

Study	Number of patients/ HIPEC procedures	Optimal* debulking achieved n (%)	HIPEC agent (procedures)	Median OS (months)°	Survival at 1/3/5 years (%)	Survival without recurrence	Univariate analysis for survival
Bakrin *et al.* (2013)	36/39	32 (89)	Platinum based (33) MMC + Platinum (9) Oxaliplatin (8) MMC (3)	Not reached	100/71.5/57.4	DFS at 1/3/5 years (%) 59.5/40/24	PCI
Sun *et al.* (2016)	22/25	15 (68)	CDDP + DOX (10) CDDP + MMC (6) paclitaxel + lobaplatin (6)	31 (95% CI: 22.3-39.7)	100/45.5/27.3	N/R	PCI>15 (HR=13.1 95% CI: 2.7-63.4)
Sardi *et al.*	30/32	28 (93)	Carboplatin (13) MMC (7) CDDP + DOX (5) Melphalan (5) MMC + DOX (1) 5-FU + MMC (1)	68 (95% CI: 0-149)	90/68/55	Median: 62 months (95% CI: 43-82) PFS at 1/3/5 years (%) 80/75/59	PCI>20 (HR=1.13 95% CI: 1.02-1.25)

*Optimal debulking was defined as residual tumor <0.25 cm; °early postoperative deaths (on days 25, 29 and 45) were excluded from calculations of median follow-up. IP, intraperitoneal; OS, overall survival; PFS, progression-free survival; DFS: disease-free survival; CI, confidence interval; N/R, not reported; HIPEC, hyperthermic intraperitoneal chemotherapy; HR, hazard ratio; PCI, peritoneal carcinomatosis index.

explained by the utilization of aggressive cytoreduction. Generally, extensive cytoreduction correlates with better survival and better response to chemotherapy.[27] However, in the gynecologic oncology literature, optimal cytoreduction is defined as <10 mm,[28] while surgical oncology considers optimal cytoreduction ≤2.5 mm. The surgical oncology standards were established based on the optimal penetration of IP chemotherapy into tumor nodules, less than 3 mm in size.[24] We were able to obtain a complete cytoreduction (CC 0-1) in 93% of patients, which translates to residual disease less than 2.5 mm or no visible tumor remaining.

Even though complete cytoreduction is considered of paramount importance in OC and PPC patients, it is still not routinely achieved. In the gynecologic surgery literature, the rate of cytoreduction with no visible disease is quite variable among surgeons with a range of 8-31%.[29,30] One explanation could be that the difficult cytoreduction in areas of the upper abdomen, such as retrohepatic vena cava, crus of diaphragm, foramen of Winslow, peripancreatic, perigastric and perisplenic areas, requires special expertise unfamiliar to even experienced gynecologic oncologists. In order to achieve a higher level of cytoreduction, a close collaboration of surgical and gynecologic oncologists may be required.

Conclusions

CRS/HIPEC is a promising treatment approach for patients with PPC. We suggest evaluation of PPC patients in a peritoneal surface malignancy center to assess the feasibility of CRS/HIPEC, as the primary treatment modality. Patients who progress following traditional treatment modalities should be considered candidates for salvage CRS/HIPEC, as well. A prospective randomized study comparing CRS followed by intraperitoneal/IV adjuvant chemotherapy with CRS/HIPEC followed by IV adjuvant chemotherapy for advanced stage (III/IV) ovarian, fallopian tube, and primary peritoneal cancers has begun in our institution with collaboration of surgical and gynecologic oncologists.

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