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II.c) Colorectal / Gastric / Other digestive peritoneal metastases

C01
CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY COMBINED WITH LIVER RESECTION FOR CONCURRENT PERITONEAL CARCINOMATOSIS AND HEPATIC METASTASIS OF GASTROINTESTINAL AND GYNECOLOGICAL PRIMARY TUMORS

P. Horvath, S. Beckert, F. Struller, A. Koenigsrainer, I. Koenigsrainer

University Hospital Tuebingen, Comprehensive Cancer Center, Tuebingen, Germany - Tuebingen (Germany)

Objectives

Surgical treatment for patients with hepatic and peritoneal metastases from gastrointestinal und gynecological tumors is still controversial. Earlier reports suggested that these patients are not eligible for a curative surgical approach. The aims of this study were to review the outcomes for patients who underwent cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy and liver resection for hepatic and peritoneal metastases.

Methods

This was a retrospective analysis of patients who underwent cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy and liver resection for metastases between 2006 and 2016. From a prospectively collected database the characteristics and survival of patients as well as morbidity- and mortality rates were analyzed.

Results

There were 40 patients who underwent this bidirectional surgical approach. The vast majority of primary tumors were of colorectal (n = 17; 43%) and of gynecological origin (n = 13; 33%). Median PCI was 14 (range, 0–39). In most patients macroscopic complete cytoreduction (CC-0) was achieved (n = 28; 70%). The median number and size of liver metastases was 1 (range, 1–3 lesions) and 2 cm (range, 0.5–6.5 cm). Morbidity rate was 55% with a reoperation rate of 25%. There was no 30- and 90-day mortality. After a median follow-up of 23 months (range, 5–92 months) 17 patients (43%) developed recurrent disease (5 peritoneal and 8 hepatic recurrences). Median overall survival for colorectal primaries was 20 months (range, 5–60 months) and for ovarian cancer 30,5 months (range, 12–58 months).

Conclusion

Simultaneous resection of hepatic and peritoneal metastases seems to offer long-term survival to highly selected patients. Nevertheless, the high morbidity rates and the high incidence of recurrent disease must be taken into consideration.

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C02
CAN MACHINE LEARNING PREDICT RESECABILITY OF A PERITONEAL CARCINOMATOSIS?

A. Maubert, L. Birtwisle, J.L. Bernard, E. Benizri, J.M. Bereder

Chirurgie Générale et Cancérologie Digestive - Nice (France)

Objectives

About 20% of initially eligible patients in a HIPEC procedure, eventually underwent simple surgical exploration. These procedures are named "Open & Close", represent up to 48%. The objective of this study was to predict the resecability of the peritoneal carcinomatosis by using a model of machine learning for decision-making support, at eligible patients in a procedure of HIPEC.

Methods

The study was conducted as an intention to treat, based on three databases including a prospective, between January 2000 and December 2015. A propensity score allowed to obtain two groups of comparable and matched patients. Then, several algorithms models of classification were studied (simple classification, conditional tree, SVM, Random Forest) to determine the model having the best performance and accuracy.

Results

Two groups of 155 patients were obtained, one group without resection and one group with. Nine criteria of non-resecability have been retained, reflecting the organ involvement. They were coded according to their importance. Five classification algorithms were tested. Training data included 218 patients and test data 92. The Random Forest model was the best performance with an accuracy close to 98%. Only two errors of prediction were observed.

Conclusion

A largest number of patients will allow improving the precision prediction. Gathering more data such biologic, radiologic even coelioscopic features, should improve the knowledge of disease and decrease the number of "Open & Close" procedures.

C03
LGR5 EXPRESSION PREDICTS PERITONEAL RECURRENCE AFTER COMPLETE RESECTION OF PRIMARY COLON CANCER

H. Nagata[1], S. Ishihara[2], T. Tanaka[1], K.Hata[1], K. Kawai[1], H. Nozawa[1]

[1]Department of Surgical Oncology, The University of Tokyo - Tokyo (Japan), [2]Surgery Department, Sanno Hospital, International University of Health and Welfare - Tokyo (Japan)

Objectives

The prognosis of patients with peritoneal metastasis remains generally dismal. To clarify whether a putative cancer stem cell marker could be an indicator of postoperative peritoneal recurrence of colon cancer.

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Methods

The expression of four cancer stem cell markers (CD133, CD44 variant 6, aldehyde dehydrogenase-1 and leucine-rich repeating G-protein coupled receptor-5 (LGR5)), was evaluated immunohistochemically in primary tumor samples from 298 patients who underwent curative resection for non-metastasized T4 colon cancer at the University of Tokyo Hospital between 1997 and 2015.

Results

The expression of none of these markers was related to overall survival or relapse-free survival. However, the time to peritoneal recurrence was significantly higher in LGR5-negative cases (five-year cumulative incidence: 13.5 vs. 46.4%, $p = 0.002$). Multivariable analysis confirmed that negative LGR5 expression was an independent risk factor for peritoneal recurrence (hazard ratio (HR) 3.72, $p < 0.001$) in addition to poor differentiation (HR: 3.61, $p = 0.044$), lymph node metastasis (HR 3.14 for N1 and 3.88 for N2, $p = 0.016$), preoperative carcinoembryonic antigen >5 ng/mL (HR 2.50, $p = 0.017$), and anastomotic leakage (HR 5.08, $p = 0.046$). The addition of LGR5 to standard clinical findings significantly improved the predictive value of the multivariable model (continuous net reclassification improvement: 0.232, $p = 0.032$: integrated discrimination improvement: 0.058, $p = 0.032$).

Conclusion

The absence of LGR5 expression was a significant predictor of peritoneal recurrence in patients with T4 colon cancer. LGR5 might be a promising biomarker to identify patients at high risk of postoperative peritoneal metastasis.

C04

INTRAPERITONEAL CHEMOTHERAPY WITH PACLITAXEL AND S-1 PLUS OXALIPLATIN FOR GASTRIC CANCER WITH PERITONEAL METASTASIS

H. Yamaguchi[1], H. Ishigami[2], R. Kanamaru[3], H. Ohzawa[3], S. Matsumoto[3], K. Kurashina[3], Y. Haruta[3], Y. Hosoya[3], H. Fujii[3], N. Sata[3], J. Kitayama[3]

[1]Dept. of Clinical Oncology, Jichi Medical University - Tochigi (Japan), [2]Dept. of Chemotherapy, the University of Tokyo - Tokyo (Japan), [3]Dept. of Surgery, Jichi Medical University - Tochigi (Japan)

Objectives

From January 2016, we introduced SOX+intraperitoneal (IP) paclitaxel (PTX) chemotherapy for gastric cancer with peritoneal metastasis. Herein, we report the treatment results.

Methods

Primary gastric cancer patients who had macroscopic peritoneal metastasis which was confirmed by staging laparoscopy or with positive cytology were enrolled. PTX was IP administered through the IP access port at 40 mg/m^2 on days 1 and 8. Oxaliplatin (L-OHP) was IV administered at 100 mg/m^2 on day 1 and S-1 was administered at 80 mg/m^2 for 14 consecutive days, followed by 7 days of rest

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Results

From Jan 2016 to Mar 2018, 29 patients were enrolled. The median follow-up period was 392 days (range, 34–820). The median number of treatment courses was 14 (1–29). L-OHP was suspended in 22 patients due to toxic effects of peripheral neuropathy or bone marrow suppression (5 courses, 1–14). The 1-year overall survival rate was 88% and median survival time was 19.7 months. Malignant ascites disappeared in 11 of 15 (73%) patients. Eighteen patients of 20 who had showed positive peritoneal washing cytology at staging laparoscopy turned out negative (90%). The frequent grade 3 or 4 toxic effects were neutropenia (38%), leukopenia (10%), and anemia (3%). Three patients underwent total gastrectomy due to perforation or stenosis of primary lesion during IP chemotherapy, all of whom had no peritoneal metastasis at the operation. Ten out of the rest 26 patients underwent gastrectomy after confirming improvement of peritoneal metastasis by second look laparoscopy. Complications associated with the intraperitoneal access port were 4 cases of infection (14%) and 3 cases of ascites reflux into subcutaneous space (10%), which were higher in frequency compared with previous reports.

Conclusion

Although SOX+IP PTX treatment is promising for gastric cancer with peritoneal metastasis, the management of intraperitoneal access port is important to perform the treatment safely.

C05

INCREASED PREVALENCE OF SECOND PRIMARY CANCERS IN PATIENTS WITH APPENDICEAL ADENOCARCINOMA

N. Pozzi, M. Cahan, B. Switzer, L. Lambert

University of Massachusetts Medical School - Worcester (United States)

Objectives

Adenocarcinomas of the appendix are rare, representing only 0.08% of all cancers and 0.4% of cancers of the gastrointestinal tract. The purpose of this study was to identify increased prevalence of second primary cancers among patients with appendiceal cancer.

Methods

Patients diagnosed with appendiceal adenocarcinoma who were also found to have a second primary cancer were identified in the SEER 18 database (1973–2014). The prevalence of the second primary cancers was analyzed and compared to the reported prevalence in the US based on NIH and SEER prevalence data.

Results

All cancers analyzed except for breast cancer were found to have a significantly increased prevalence among appendiceal cancer patients (Table). The increased prevalence was greatest for colorectal cancer with at 6.6% vs 0.39% and 0.41% the US prevalence reported by SEER and NIH, respectively.

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All cancers with the exception of breast cancer are found to have an increased prevalence among patients found to have appendiceal adenocarcinoma.

2nd Primary	Cases	Prevalence of 2nd Primary Concomitant Appendix Cancer	Prevalence of 2nd Primary in US Population	P-value
Melanoma	42	0.74	0.36	P = 0.000043
Colorectal	367	6.46	0.41	P = <0.00001
Breast	115	2.02	2.06	P = 0.61
Lung	62	1.09	0.16	P = <0.00001
Esophageal	9	0.16	0.01	P = 0.000273
Gastric	22	0.39	0.03	P = <0.00001
Pancreatic	20	0.35	0.02	P = <0.00001
Small bowel	37	0.65	0.03	P = <0.00001
Lymphoma	34	0.60	0.27	P = 0.000142
Sarcoma	11	0.19	0.07	P = 0.019
Prostate	192	3.38	0.95	P = <0.00001
Ovarian	41	0.70	0.14	P = <0.00001
Cervix and Uterus	43	0.76	0.08	P = <0.00001

Conclusion

A high-level of suspicion of second primary malignancies, particularly colon cancer, should be employed for patients diagnosed with appendiceal adenocarcinoma. Screening for colon cancer should be considered in the appropriate setting for all patients with appendiceal cancer. Genomic testing of appendiceal cancers may provide profiles predictive of increased cancer risk.

C06

BREAST CANCER PERITONEAL METASTASIS-ROLE OF CYTOREDUCTIVE SURGERY & HIPEC

J. Spiliotis[1], A. Prodromidou[2], D. Farmakis[1], T. Metaxas[1], A. Ntinas[1], P. Koustas[1], H. Chalkidis[1], A. Christopoulou[3]

[1]European Interbalkan Medical Center - Thessaloniki (Greece), [2]Department of Surgery "Metaxa" Memorial Cancer Hospital - Piraeus (Greece), [3]Department of Medical Oncology "St. Andrews" Hospital - Patras (Greece)

Objectives

Peritoneal metastases from breast cancer are extremely rare. The literature provides no information regarding this infrequent event and its management. We present outcomes in four patients (mean age 53 years) with peritoneal metastasis from breast cancer with no evidence of liver, bone or lung deposits.

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Methods

Patients were treated with cytoreductive surgery (CRS) plus HIPEC by the closed technique at 42, 5°C for 60 minutes with cisplatin 100 mg/m^2 and paclitaxel 175 mg/m^2.

Histopathology of the primary breast cancer was ductal carcinoma in two of them while in the rest was lobular carcinoma.

Results

Mean peritoneal cancer index (PCI) was 16. In 50% of the cases complete cytoreduction was achieved.

One patient died of the disease at 54 months. Three are alive and disease free at 68, 78 and 12 months, respectively.

Conclusion

These results encouraging that CRS & HIPEC is a promising approach which merits investigation in larger series.

C07

CYTOREDUCTION SURGERY WITH HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY: APPRAISAL OF OUTCOMES IN A NEWLY EMERGING ALGERIAN CENTER

M.A. Abid

Centre de Lutte Contre le Cancer de Batna - Batna (Algeria)

Objectives

Described since the 1990s the results of cytoreduction surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) are well defined in experienced centers. Outcomes of this demanding procedure in a new center need to be reported. To evaluate morbidity and mortality and to demonstrate the long learning curve needed to master this procedure in a new specialized center in Algeria.

Methods

This is a retrospective review of a prospectively maintained database; between December 2015 and February 2018, patients with peritoneal malignancies (PM) of primitive or secondary origin undergoing CRS/HIPEC were enrolled.

Results

The study included 78 patients, 54 are women (69.23%) and 24 men (30.77%), with an average age of 48, 38 years (21–75 range). The most common histology of PM was Pseudo myxoma (41), followed by carcinomatosis of colorectal origin (27), carcinomatosis of ovarian origin (9), and one mesothelium. In most patients CRS was completed 58 patients (74.35%), with 45 patients undergoing digestive anastomoses. The mean operative time (CRS+HIPEC) was 335.37 min and the median length of hospital stay was 12.78 days. Morbidity and mortality were 24.35% and 8.9% respectively. Major morbidity was defined as an event of grade III Dindo-Clavien 20 patients. Till today, 51 patients (65.38%) are living without recurrence.

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Conclusion

CRS with HIPEC provide a promising approach despite a long learning curve and a relatively high postoperative morbidity and mortality rate in a new emerging center. A more selective pre and intraoperative judgment on who undergoes CRS/HIPEC is adopted to reduce the morbimortality.

C08

NEOADJUVANT CHEMOTHERAPY FOLLOWED BY CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR COLORECTAL CANCER: A FEASIBILITY AND SAFETY STUDY

M. Leimkühler, P.H. Hemmer, A.K. Reyners, D.J. De Groot, R.J. Van Ginkel, L.B. Been, G.H. De Bock, B.L. Van Leeuwen

University Medical Center Groningen - Groningen (Netherlands)

Objectives

Standard treatment for colorectal peritoneal carcinomatosis (PC) typically involves cytoreductive surgery (CRS), hyperthermic intraperitoneal chemotherapy (HIPEC), and if possible, postoperative adjuvant chemotherapy. However, a substantial percentage of patients never receive adjuvant chemotherapy because of postoperative complications. Neoadjuvant chemotherapy could be beneficial in this setting, so we assessed its feasibility and safety when used before CRS and HIPEC.

Methods

In this non-randomized, single-center, observational feasibility study, patients were scheduled to receive six cycles of capecitabine and oxaliplatin before CRS and HIPEC. Computed tomography was performed after the third and sixth chemotherapy cycles to evaluate tumor response, and patients underwent CRS and HIPEC if there were no pulmonary and/or hepatic metastases. Postoperative complications, graded according to the Clavien–Dindo classification, were compared with those of a historic control group that received postoperative adjuvant chemotherapy.

Results

Of the 14 patients included in the study, 4 and 3 had to terminate neoadjuvant chemotherapy early because of toxicity and tumor progression, respectively. CRS and HIPEC were performed in 8 patients, and the timing and severity of complications were comparable to those of patients in the historic control group treated without neoadjuvant chemotherapy.

Conclusion

Patients with peritoneal metastases due to colorectal carcinoma can be treated safely with neoadjuvant chemotherapy before definitive therapy with CRS and HIPEC.

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C09
STRATEGIES FOR MANAGING INTRAOPERATIVE DISCOVERY OF LIMITED COLORECTAL PERITONEAL METASTASES

A. Mariani, M. Gelli, I. Sourrouille, L. Benhaim, M. Faron, C. Honoré, D. Elias, D. Goéré

Gustave Roussy Cancer Campus - Department of Surgical Oncology - Villejuif (France)

Objectives

Management of limited synchronous peritoneal metastases of colorectal cancer (CRPM) is critical to outcome. Resection of the primary tumor and CRPM can be done concurrently, followed by hyperthermic intraperitoneal chemotherapy (HIPEC) either immediately during the same procedure (one-stage), or during a systematic second-stage procedure (two-stage). The aim of the study was to compare these two strategies for morbi-mortality and survival in limited synchronous CRPM.

Methods

All patients presenting with limited (initial peritoneal cancer index [PCI] ≤10) synchronous CRPM who had undergone complete cytoreductive surgery plus HIPEC between 2000 and 2016 were selected from a prospectively-maintained institutional database.

Results

Seventy-four patients were included, 31 in the one-stage group, and 43 in the two-stage. During second-stage surgery, a peritoneal recurrence was diagnosed in 86% of patients. Among them, 12 patients (28%) had a PCI >10 and two could not undergo HIPEC because of disseminated and unresectable peritoneal disease (PCI 18 and 26). Regarding one-stage surgery, peritoneal recurrence occurred in 29% after a mean of 23 months. Overall survival at 1, 3 and 5 years was similar between the two groups, 96%, 59% and 51% for the one-stage group, and 98%, 77% and 61% for the two-stage. PCI >10 at the time of HIPEC and liver metastases were independent negative prognostic factors.

Conclusion

This is the first study to compare these two strategies. For limited and synchronous CRPM diagnosed fortuitously, one-stage curative treatment is preferable, avoiding an extra surgical procedure. The two-stage strategy carries a risk of early peritoneal recurrence as more extensive and unresectable disease.

C10

CYTOREDUCTION SURGERY WITH HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY IN METASTATIC PERITONEAL HEPATOCELLULAR CARCINOMA WITH HIGH PCI

K.C. Hung[1], Y.Y. Wang[2], G.C. Huang[3], Y.F. Chen[4]

[1]Department of Surgery, Yuan's General Hospital - Kaohsiung (Taiwan, Republic of China), [2]Hyperthermic center, Yuan's General Hospital - Kaohsiung (Taiwan, Republic of China), [3]Division of Hemato-oncology, Department of Internal Medicine, Yuan's General Hospital - Kaohsiung (Taiwan, Republic of China), [4]Department of Education and Research, Yuan's General Hospital - Kaohsiung (Taiwan, Republic of China)

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Objectives

Effective treatment for peritoneal metastases of hepatocellular carcinoma (HCC) has not yet been established. Although cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) have shown favorable outcomes in certain malignancies, their role in peritoneal HCC is not clear. We present a series of patients with peritoneal metastatic HCC treated with CRS and HIPEC and evaluate the outcomes of the combination treatment.

Methods

Between Sep/2015–Dec/2016, 6 patients with peritoneal metastatic HCC underwent CRS and HIPEC. We assessed the clinical course and outcome of these patients to determine the effectiveness of the treatment and the factors related to survival. The selection criteria for CRS and HIPEC included: resectable peritoneal metastatic tumors, HCC in the liver being under control or resectable, Child's A liver disease, good ECOG performance (0–1), adequate renal and heart function. Following cytoreduction surgery, HIPEC was performed with the closed abdomen technique. Perfusion with Mitomycin C at a dose of 35 mg /m^2 and at a flow rate of 1 liter/minute was then initiated with 50% of the dose perfused initially, 25% at 30 minutes, and 25% at 60 minutes. The total HIPEC time was 90 min at intraabdominal temperature of 40°C (104°F).

Results

Between Sep/2015–Dec/2016, six patients with extensive disease to the peritoneum underwent CRS and HIPEC. Three patients were man. Mean age was 59.3 (35–69). ECOG was 0. Mean PCI was 18 (8–25). Except the intra-hepatic metastases, complete macroscopic cytoreduction (CCR 0-1) was achieved in all patients. There was no post-operative mortality at 30 days. Four patients died and two patients are alive with disease in the liver. Median survival was 15.67 months. One-year survival rate was 66.7%, and two-year was 25.0%. CT-PCI was less than 3 in the last CT/MRI image studies. The causes of death were HCC recurrence in the liver or lung metastasis.

Conclusion

The combination treatment of CRS and HIPEC is safe and effective to remove peritoneal tumors of HCC. It can be considered in patients with adequate preservation of liver function. It should be done as early as possible to decrease the risk of tumor spread via blood or lymphatic routes.

C11
RISK FACTORS FOR MORBIDITY, MORTALITY AND PROLONGED LENGTH OF STAY AFTER CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY

M. Bailon-Cuadrado, E. Asensio-Diaz, B. Perez-Saborido, P. Pinto-Fuentes, I. Gonzalez-Blanco, D. Pacheco-Sanchez

Rio Hortega University Hospital - Valladolid (Spain)

Objectives

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is nowadays considered the standard of treatment for peritoneal carcinomatosis from several origins, regardless it has very high morbidity and mortality rates. The aim of our work was to analyse morbidity, mortality and length of stay (LOS) in our sample of treated patients and find out which factors are linked to their appearance.

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Methods

A prospective study was carried out with patients who underwent CRS and HIPEC for peritoneal carcinomatosis between January 2015 and June 2017 at our institution. Surgery was performed 4–6 weeks after last chemotherapy session. Complications were carefully collected during the first 60 days of postoperative period. We evaluated several preoperative and intraoperative variables and their relation to morbidity (overall, severe and anastomotic leakage), mortality and LOS.

Results

Finally, 74 patients (90.5% women) were analysed. Mean age was 57.24 ± 8.67 years. Most frequent aetiologies were: ovarian cancer (50.0%) and colorectal cancer (25.7%). Median surgical peritoneal cancer index was 11. HIPEC and bidirectional chemotherapy were associated to CRS in 83.8% and 43.2%, respectively. Overall and severe complications appeared in 33 (44.6%) and 20 (27.0%) patients, respectively. Anastomotic leakage took place in 8 (17.8%) of 45 patients with anastomosis. Mortality happened in 3 (4.05%) patients. Median LOS was 13.5 days. After performing multivariate analysis, statistically significant variables were: HIPEC (OR = 15.5, 95% CI: 1.5–160.6, p = 0.021) and proctectomy (OR = 3.3, 95% CI: 1.1–9.5, p = 0.029) for overall complications, bidirectional chemotherapy (OR = 3.7, 95% CI: 1.2–11.8, p = 0.025) and surgical time (OR = 1.006, 95% CI: 1.001–1.011, p = 0.021) for severe complications, proctectomy (OR = 1.4, 95% CI: 1.1–1.8, p = 0.011) for anastomotic leakage, gastrectomy (OR = 26.4, 95% CI: 2.0–343.9, p = 0.012) for mortality, surgical time (OR = 1.008, 95% CI: 1.003–1.013, p = 0.003) and cholecystectomy (OR = 4.9, 95% CI: 1.5–16.5, p = 0.011) for prolonged LOS (≥14 days).

Conclusion

We can conclude that, in our sample of patients, gastrectomy is associated to mortality, proctectomy to overall complications and anastomotic leakage, surgical time to severe complications and prolonged LOS, intraperitoneal chemotherapy to both overall and severe complications, and cholecystectomy to prolonged LOS. Further homogeneous and multicentric studies are needed to assess the risk factors for short-term outcomes.

C12
HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) IN COMBINED TREATMENT OF LOCALLY ADVANCED AND INTRAPERITONEALY DISSEMINATED GASTRIC CANCER: A RETROSPECTIVE COOPERATIVE CENTRAL-EASTERN EUROPEAN STUDY

R. Yarema[1], J. Mielko[2], T. Fetsych[1], M. Ohorchak[3], K. Rawicz-Pruszynski[2], T. Jastrzebski[4], P. Hyrya[3], Y. Kovalchuk[3], V. Safiyan[3], I. Karelin[3], A. Mashukov[5], V. Maksimovsky[5], V. Kopetskiy[6], Y. Kondratskiy[6], M. Paskonis[7], W. Polkowski[2]

[1]Danylo Halytsky Lviv National Medical University - Lviv (Ukraine), [2]Medical University of Lublin - Lublin (Poland), [3]Lviv State Oncological Regional Center - Lviv (Ukraine), [4]Medical University of Gdansk - Gdansk (Poland), [5]Odessa National Medical University - Odessa (Ukraine), [6]National Cancer Institute - Kyiv (Ukraine), [7]Vilnius University Hospital Santaros Klinikos - Vilnius (Lithuania)

Objectives

Clinical experience in Western Europe suggests that cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) play an important role in the management of gastric cancer (GC) with peritoneal metastases (PM). The aim of this study was to create a clinical registry of patients from Central and Eastern Europe as well as analyze short- and long-term outcomes.

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Methods

Data were collected from 6 (out of 13 invited) Central-East European HIPEC centers that have had experience with GC patients. HIPEC was used in 117 patients (56 male, 61 female; ages from 22 to 75, with a median 55 years) for the following indications:

1. Treatment of GC with overt PM n = 70 (therapeutic group)

2. Adjuvant/proactive setting after potentially radical resections of locally-advanced GC with high risk of intraperitoneal progression n = 37 (adjuvant group)

3. Palliative approach for elimination of intense ascites without gastrectomy n = 10 (palliative group)

Results

Thirty-five patients (30%) were recorded as having postoperative complications, including surgical morbidity (18%), necessitating re-laparotomy in 17 patients (14,5%). HIPEC-related toxicity grade III–IV was found in 8 patients (7%), while somatic morbidity occurred in 9 patients (8%). Postoperative mortality was 5%. Median overall survival in the groups with therapeutic, adjuvant, and palliative indications was 12.6, 34, and 3.5 months. Median relapse-free survival for the three groups were 10, 28, and 3 months, respectively. The only long-term survivors occurred in the group with PCI of 0–6 points (without survival difference in groups with PCI 7-12 vs PCI 13 or more points).

Conclusion

GC patients with limited PM can benefit from CRS and HIPEC. HIPEC is a well-tolerated and effective method of adjuvant treatment of GC with high risk of intraperitoneal progression.

C13
CYTOREDUCTIVE SURGERY PLUS HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY IN TREATING PATIENTS WITH PERITONEAL CARCINOMATOSIS: THE GREEK EXPERIENCE

J. Spiliotis[1], N. Kopanakis[2], A. Terras[2], A. Prodromidou[2], M. Ferfelis[3], A. Raptis[3], N. Zampitis[3], I. Kyriazanos[4], A. Christopoulou[5], E. Efstathiou[2]

[1]a. 1st Department of Surgery, Metaxa Memorial Cancer Hospital, Piraeus b. Surgical Oncology and HIPEC Department, Athens Medical Centre c. Surgical Oncology and HIPEC Department, European Interbalkan Medical Centre, Thessaloniki - Athens (Greece), [2]1st Department of Surgery, Metaxa Memorial Cancer Hospital, Piraeus - Athens (Greece), [3]Surgical Oncology and HIPEC Department, Athens Medical Centre - Athens (Greece), [4]2nd Department of Surgery, Naval and Veterans Hospital - Athens (Greece), [5]Department of Medical Oncology, "Agios Andreas" Hospital - Patras (Greece)

Objectives

Several studies have shown the benefits of cytoreductive surgery (CRS) plus HIPEC when treating peritoneal carcinomatosis from digestive, primary peritoneal and other types of cancer. We provide the experience and results from 3 different surgical institutions in Greece.

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Methods

We retrospectively analyzed 418 patients that underwent CRS plus HIPEC, from September 2008 to March 2018. Patient demographics and operative characteristics were recorded for all. Primary end points were overall survival, progression free and disease free survival. Secondary end points were morbidity and mortality. A univariate and multivariate analysis was performed to correlate factors.

Results

Median age was 53 years old and 72% of patients were females. Primary tumors were 24% from colorectal origin, 36% ovarian cancer, 5% gastric cancer, 15% pseudomyxoma peritonei, 6% peritoneal mesothelioma and 14% were other tumors (endometrial, pancreatic, breast, sarcoma). Median Peritoneal Cancer Index (PCI) was 15 and 61% of patients achieved a complete cytoreduction (cc-0). Severe complications (Clavien – Dindo III/IV) occurred in 163 patients (39%) and 90-day mortality was 5%. Median overall survival was 33 months for all patients and 1,3,5-year survival rates were 88%, 45% and 24% respectively. Patients with PC from colorectal cancer had a median survival of 26 m, ovarian cancer 36 m, gastric cancer 14 m, pseudomyxoma peritonei 49 m, peritoneal mesothelioma 38 m and for other cancers 22 m. When analyzed in a univariate analysis, PCI and cc score were significantly correlated ($p < 0.001$) with overall survival and when in multivariate analysis, PCI and cc score remained correlated significantly ($p < 0.5$).

Conclusion

Cytoreductive surgery in combination with HIPEC is a feasible and beneficial method in treating patients with peritoneal carcinomatosis. It can be done with acceptable morbidity and mortality rates. Appropriate case selection by a multi-disciplinary team is vital to achieve complete cytoreduction and optimize outcomes.

C14
THE ROLE OF CHEMOTHERAPY IN THE SETTING OF RESECTABLE PERITONEAL CARCINOMATOSIS OF COLORECTAL ORIGIN

G. Liberale[1], A. Hendlisz[2]

[1]Surgery, Institut J. Bordet (U.L.B.) - Brussels (Belgium), [2]Medical Oncology, Institut J. Bordet (U.L.B.) - Brussels (Belgium)

Objectives

Therapeutic decision-making concerning the use of neoadjuvant and adjuvant chemotherapy in peritoneal carcinomatosis (PC) of colorectal cancer (CRC) origin is often difficult.

The objective of this study was to evaluate the attitudes of Belgian and International oncologists with regard to the role of chemotherapy in this setting.

Methods

An anonymous survey including 5 questions about the use of neoadjuvant and/or adjuvant chemotherapy in resectable PC of CRC origin was sent by mail to Belgian oncologists and International experts in PC (PSOGI group).

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Results

84 oncologists or surgical oncologists responded to the survey. A total of 41.66% reported being involved occasionally (1–15 patients/year) and 54.76% frequently (>15 patients/year) in making therapeutic decisions regarding PC of CRC origin. Systemic neoadjuvant chemotherapy would be recommended by 53% and not recommended by 47%. Interestingly, 59% would propose systemic adjuvant chemotherapy, 26.5% would propose chemotherapy in cases of response to neoadjuvant chemotherapy, and 14.5% would never propose adjuvant chemotherapy. Thirty-one percent of oncologists reported that their decisions were based on specific evidence in the literature, while 58% based decisions on similar clinical situations, and 11% did not have a basis for their decisions. A majority of oncologists, 91%, agreed that decision-making in this setting is never easy and that more clear recommendations are needed.

Conclusion

Results of this survey show that the use of neoadjuvant and adjuvant chemotherapy in resectable patients with PC of CRC origin varies and that the majority of oncologists need more clear recommendations.

C15
FEASIBILITY, SAFETY, TOLERABILITY, AND PRELIMINARY EFFICACY OF REPETITIVE LAPAROSCOPIC EPIPAC WITH OXALIPLATIN FOR ISOLATED UNRESECTABLE COLORECTAL PERITONEAL METASTASES: PRELIMINARY RESULTS OF A MULTICENTRE, SINGLE-ARM PHASE II STUDY

K. Rovers[1], R. Lurvink[1], E. Wassenaar[2], R. Wiezer[2], D. Boerma[2], J. Nederend[3], G.J. Creemers[4], S. Nienhuijs[1], I. De Hingh[1]

[1]Surgery, Catharina Hospital, Netherlands - Eindhoven (Netherlands), [2]Surgery, St. Antonius Hospital, Netherlands - Nieuwegein (Netherlands), [3]Radiology, Catharina Hospital, Netherlands - Eindhoven (Netherlands), [4]Medical Oncology, Catharina Hospital, Netherlands - Eindhoven (Netherlands)

Objectives

To investigate the feasibility, safety, tolerability, and preliminary efficacy of repetitive laparoscopic electrostatic pressurised intraperitoneal aerosol chemotherapy with oxaliplatin (ePIPAC-OX) for isolated unresectable colorectal peritoneal metastases.

Methods

This is a multicentre, single arm phase 2 study. Eligible patients are adults with a good performance status (WHO 0-1), histological or cytological confirmation of a colorectal carcinoma in peritoneal deposits or ascites, and unresectable disease determined by laparotomy or laparoscopy. Exclusion criteria are the presence of extraperitoneal metastases, a symptomatic presentation (e.g. bowel obstruction), any contraindication for the planned chemotherapy (e.g. organ dysfunction), any contraindication for a laparoscopy, or previous PIPAC-procedures. Instead of standard palliative systemic therapy, included patients receive repetitive laparoscopic ePIPAC-OX (92 mg/m^2) with a simultaneous intravenous bolus 5-fluorouracil (400 mg/m^2) and leucovorin (20 mg/m^2), repeated with an interval of six weeks. Four weeks after each procedure, patients are radiologically, biochemically, and clinically evaluated. In case of stable disease or disease response, a next PIPAC-procedure is planned. In case of disease progression or symptomatic disease, standard palliative systemic therapy is restarted. The primary endpoint of the study is the number of patient with severe toxicity (CTCAE >2) up to four weeks after the last procedure. Secondary endpoints are the feasibility of accrual,

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environmental safety, pharmacokinetics of oxaliplatin, intraoperative characteristics, intraoperative complications, moderate toxicity up to four weeks after the last procedure, hospital stay, readmission rate, the number of procedures in each patient and reasons for discontinuation, macroscopic tumour response, histological tumour response, radiological tumour response, biochemical tumour response, quality of life, costs, the number of patients who undergo secondary cytoreductive surgery, intraperitoneal progression free survival, systemic progression free survival, and overall survival.

Results

Between November 2017 and April 2018, 15 out of 20 patients have been included in two centres. Accrual is expected to be completed in July 2018. If accepted, preliminary results of this study are presented at the congress.

Conclusion

If accepted, preliminary conclusions are presented at the congress.

C16
DIFFERENCES BETWEEN PERITONEAL METASTASES AND LOCAL RECURRENCE FROM COLORECTAL CANCERS AFTER CYTOREDUCTIVE SURGERY AND HIPEC

F. Dumont[1], S. Joseph[1], G. Lorimier[1], V. De Franco[1], R. Werner[1], V. Verriele[2], O. Kerdraon[2], J. Raimbourg[3], H. Senellart[4], O. Campion[5], O. Capitain[5], V. Guerin-Meyer[6], J.L. Raoul[6], S. Hiret[6], E. Thibaudeau[6]

[1]Surgical Oncology - Saint Herblain (France), [2]Pathological Oncology - Saint Herblain (France), [3]Medicall Oncology - Saint Herblain (France), [4]Medical Oncology - Saint Herblain (France), [5]Statistical Department - Saint Herblain (France), [6]Medical Oncolgy - Saint Herblain (France)

Objectives

Recurrences by intra-abdominal tumor cell spread are majors problems concerning colorectal cancer (CRC). These recurrences can be divided as local (in the initial tumor bed without peritoneum after primary resection) and peritoneal recurrence (LPR) and peritoneal recurrence (PR) arising only in peritonealized areas. Tumor growth patterns between LPR and PR are different in animal models but have never been compared in clinical human study. The purpose of this study was to identify patterns of LPR and PR and prognostics factors after complete cytoreductive resection (CCR) and HIPEC.

Methods

Analyze from a prospective database of 108 CCR patients treated and HIPEC in Institut de Cancérologie de l'Ouest between 2008 and 2016.

Results

The population was divided as LPR group (presence of LR and eventually of PR), 56 patients (51.8%) and PR group (isolated PR) 52 patients (48.1%). There was no statistical difference between LPR and PR on patients characteristics (age, sex, Charlson score, ASA score) or perioperative systemic chemotherapy treatments. The median peritoneal cancer index (PCI) was respectively 6 and 4 ($p = 0.485$) in PR and LPR group. The median number of organs resected for tumor involvement (respectively, 2 vs 1; $p < 0.001$) and

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the rate of patient with metastatic lymph node (LN) from resected organ (respectively, 25% vs 7% (p = 0.016)) were significantly more important in LPR than in PC group.

The 3 years overall survival (OS) and disease-free survival (DFS) rates were respectively 55% vs 69% (p = 0.262) and 21% vs 21% (p = 0.782) in LPR and PC group. Multivariate analysis showed that the PCI was the only prognostic factor of OS. Age, Charlson score, type of recurrence, primary tumor location, primary TN stage, neoadjuvant or adjuvant chemotherapy treatment, LN involvement of resected organ had no impact on survival.

Conclusion

Our results confirm that the peritoneum is an oncologic barrier to local tumor progression. The peritoneum limits the organ and lymph node involvement. A lymph node involvement of invaded organ is frequent (25%) in case of LPR and rare in PR (7%). After CCR and HIPEC, type of recurrence (LPR or PR) has no impact on long term survival but optimal surgical resection with lymphadenectomy of invaded organ by LR should be systematically adopted.

C17

THE CURRENT PRACTICE OF CYTOREDUCTIVE SURGERY AND HIPEC FOR COLORECTAL PERITONEAL METASTASES: RESULTS OF A WORLDWIDE WEB-BASED SURVEY OF THE PERITONEAL SURFACE ONCOLOGY GROUP INTERNATIONAL (PSOGI)

M. Bushati[1], K.P. Rovers[2], A. Sommariva[3], P.H. Sugarbaker[4], D.L. Morris[5], Y. Yonemura[6], C.A. Quadros[7], S.P. Somashekhar[8], W. Ceelen[9], P. Dubé[10], Y. Li[11], V.J. Verwaal[12], O. Glehen[13], P. Piso[14], J. Spiliotis[15], M.C.C. Teo[16], S. González-Moreno[17], P.H. Cashin[18], K. Lehmann[19], M. Deraco[20], B. Moran[21], I.H.J.T. De Hingh[2]

[1]Department of Surgery, Oncology and Gastroenterology Unit, University of Padova - Padova (Italy), [2]Department of Surgery, Catharina Hospital, P.O. Box 1350, 5602 ZA - Eindhoven (Netherlands), [3]Unit of Surgical Oncology of the Esophagus and Digestive Tract, Veneto Institute of Oncology IOV-IRCCS - Castelfranco Veneto (Italy), [4]Center for Gastrointestinal Malignancies, MedStar Washington Hospital Center - Washington, DC (United States), [5]Department of Surgery, St George Hospital, Gray St Kogarah - Sydney (Australia), [6]Peritoneal Surface Malignancy Center, Kishiwada Tokushukai Hospital, 4-27-1 Kamori-Cho - Kishiwada City, Osaka (Japan), [7]Surgical Oncology Unit, São Rafael Hospital, av. São Rafael, 2152, São Marcos - Salvador, Bahia (Brazil), [8]Department of Surgical Oncology and Robotic Surgery, Manipal Comprehensive Cancer Center, Manipal Hospital - Karnataka (India), [9]Department of Gastrointestinal Surgery, Ghent University Hospital Belgium - Gent (Belgium), [10]Department of Surgery, Hôspital Maisonneuve-Rosemont, Université de Montréal - Montreal, Quebec (Canada), [11]Department of Peritoneal Cancer Surgery, Beijing Shijitan Hospital of the Capital Medical University, - Beijing (China), [12]Department of Surgery, Aarhus University Hospital - Aarhus (Denmark), [13]Department of Surgical Oncology, Hospices Civils de Lyon and Lyon Faculty of Medicine, Lyon Sud Hospital - Lyon (France), [14]Department for General- and Visceral Surgery, Hospital Barmherzige Brüder - Regensburg (Germany), [15]European Interbalkan Medical Center - Thessaloniki (Greece), [16]National Cancer Centre Singapore - Singapore (Singapore), [17]Surgical Oncology, MD Anderson Cancer Center - Madrid (Spain), [18]Department of Surgical Sciences, Section of Surgery, Uppsala University, Akademiska Sjukhuset - Uppsala (Sweden), [19]Department of Visceral and Transplantation Surgery, University Hospital of Zurich - Zurich (Switzerland), [20]Peritoneal Surface Malignancies Unit, Fondazione IRCCS Istituto Nazionale dei Tumori - Milan (Italy), [21]Peritoneal Malignancy Institute Basingstoke, Hampshire Hospitals Foundation Trust - Basingstoke (United Kingdom)

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Objectives

At present, selected patients with resectable colorectal peritoneal metastases (CPM) are increasingly treated with a combination therapy of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). The aim of this study was to investigate the current worldwide practice.

Methods

HIPEC experts from 19 countries were invited through the Peritoneal Surface Oncology Group International (PSOGI) to complete an online survey concerning their personal expertise and current hospital and countrywide practice.

Results

It is estimated that currently more than 3800 patients with CPM (synchronous and metachronous) are annually treated with CRS and HIPEC in 430 centers. Integration of CRS and HIPEC in national guidelines varies, resulting in large treatment disparities between countries. Amongst the experts, there was general agreement on issues related to indication, surgical technique and follow up but less on systemic chemotherapy or proactive strategies.

Conclusion

This international survey demonstrates that CRS and HIPEC is now performed on a large scale for CPM patients. Variation in treatment may result in heterogeneity in surgical and oncological outcomes, emphasising the necessity to reach consensus on several issues of this comprehensive procedure. Future initiatives directed at achieving an international consensus statement are needed.

C18

CAN BASELINE QUALITY OF LIFE SCORES PREDICT FOR MORBIDITY AND SURVIVAL AFTER CRS AND HIPEC: A PROSPECTIVE STUDY

C. Chia, G. Tan, J. Ong, C. Lim, M. Teo

NCCS (Singapore)

Objectives

Various studies have shown that patients can achieve good quality of life(QoL) post cytoreductive surgery(CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Our prospective study aims to validate this as well as elucidate clinical factors that may predict for poorer QoL. We also assessed if baseline QoL is associated with morbidity and survival after surgery.

Methods

All patients who had CRS and HIPEC from February 2012 to April 2017 were included. The European Organization for the Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30) was administered to the patients at baseline prior to surgery and thereafter at 3, 6 and 12 months.

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Results

151 patients underwent 155 surgeries. 472 questionnaires were completed. Questionnaire completion was 80.0% at 3 months, 69.7% at 6 months and 54.8% at 12 months. 56.2% of tumours were colorectal or appendicael, 31.6% were ovarian and primary peritoneal, 3.9% were mesothelioma and 8.4% were others. 69 (44.5%) patients had no post-operative complications. Of the 86 patients that had complications, 21 (13.5%) were grade 3 or 4. Median disease- free survival was 16.5 months. Median overall survival was not reached. The 3 year disease free survival and overall survival were 24.0% and 73.0% respectively.Our results showed a significant increase in the global health status at 3,6 and 12 months postoperatively. The decreases in the functional scales post-operatively had recovered to baseline by 1 year. Patients with these factors were found to have a significantly lower global health status score at 6 months: PCI score ≥15, peritonectomy duration ≥430 minutes, ICU stay ≥1 day, hospital stay ≥13 days, presence of complications and patients who died within a year.Patients with lower global health status, physical functioning, role functioning scores and higher symptom summary scores at baseline were found to be more likely to develop a complication. Patients with a lower social functioning score, higher pain score and higher dyspnoea score at baseline had a significantly lower overall survival.

Conclusion

Various clinical factors can help us predict a patient's QoL post surgery. Several factors at baseline were also able to help us predict morbidity and survival. Going forward, we can use these factors to help us better select patients who will have a greater benefit from CRS and HIPEC.

C19

INTRAPERITONEAL CHEMOTHERAPY WITH PACLITAXEL FOR GASTRIC CANCER WITH PERITONEAL RECURRENCE AFTER GASTRECTOMY

D. Kobayashi, M. Kanda, C. Tanaka, M. Suenaga, H. Takami, N. Hattori, M. Hayashi, Y. Niwa, S. Yamada, G. Nakayama, M. Koike, M. Fujiwara, Y. Kodera

Nagoya University - Nagoya (Japan)

Objectives

Peritoneal recurrence is the most frequent and critical prognostic factor for advanced gastric cancer (GC) patients who undergo gastrectomy. Combination of intraperitoneal (IP) and systemic chemotherapy, which was proved to be effective for the primary GC with peritoneal metastasis in PHOENIX-GC trial, can be a promising option for GC patients with peritoneal recurrence after gastrectomy. A retrospective study was performed to evaluate the multidisciplinary treatment strategy.

Methods

GC patients with peritoneal recurrence after radical gastrectomy who were diagnosed to have no other distant metastasis were enrolled. The chemotherapy consisted of 2 weeks of oral S-1 (80 mg/m^2) and intravenous (IV) (50 mg/m^2) and IP (20 mg/m^2) administration of paclitaxel (PTX) in day 1 and day 8 in 3 weeks. PTX was administered through the implanted peritoneal access port and catheter concurrent with IV infusion. The chemotherapy has been repeated until unacceptable toxicity or disease progression.

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Results

From 2010 to 2017, a total of 8 patients were enrolled. The male/female ratio was 5/3, and the median age was 56 (33–75). 5 patients were pathologically diagnosed to be in Stage III, and 3 were in Stage IV due to resectable peritoneal metastasis and/or positive peritoneal cytology, who could achieve macroscopically curable resection consequently. 7 patients underwent systemic postoperative chemotherapy which consisted of S-1 alone or S-1 plus cisplatin. All patients were confirmed to have peritoneal recurrence spread into whole peritoneal cavity by laparoscopy. The median duration between gastrectomy and diagnosis of peritoneal recurrence was 34.6 months (15.2–62.0). The median overall survival time was 16.8 months (8.2–27.0) and the median progression-free survival time was 12.5 months (7.4–21.4) since the initiation of chemotherapy. The median time to treatment failure was 12.8 months (2.1–21.9). 3 out of 4 patients with positive peritoneal cytology before treatment showed cytology converted negative after the first treatment course. 1 out of 3 patients with ascites before treatment demonstrated decrease of ascites, and 1 out of 3 patients with hydronephrosis before treatment experienced an improvement by the treatment.

Conclusion

IP chemotherapy combined with systemic treatment is feasible and could have potential ability to prolong survival for GC patients with peritoneal recurrence after gastrectomy.

C20

PATIENT SELECTION POLICY AND PATTERN OF RECURRENCE AFTER CYTOREDUCTIVE CURGERY AND HIPEC FOR COLORECTAL CARCINOMATOSIS PLAY A ROLE ON PATIENTS' OUTCOME

M. Vaira[1], M. Robella[1], A. Cinquegrana[1], G. Gavello[1], M. De Simone[2]

[1]Unit of Surgical Oncology -Candiolo Cancer Institute FPO - Turin (Italy), [2]Unit of Surgical Oncology (Director) -Candiolo Cancer Institute FPO - Turin (Italy)

Objectives

Improvement of cure rate after cytoreductive surgery (CRS) associated to hyperthermic intraperitoneal chemotherapy (HIPEC) for patients with colorectal peritoneal carcinomatosis (PC) are described in literature. The selection policy and the pattern of recurrence play a role on outcome improvement (both on disease-free survival DFS and Overall Survival OS). Aim of the study is to present a tertiary single center results based on change of patients' selection policy.

Methods

From a database of 460 CRS+HIPEC performed between 1996 and 2017, we selected 70 patients (out of 86 treated by CRS+HIPEC) with colorectal PC. From 2004 (Group B, while "Group A" was the group of patients treated < 2004), we also excluded patients with both PCI > 16 and poor prognostic factors of primary tumor (i.e. T4, N2 and G3 especially when more than one feature was present) and only perform HIPEC in optimal cytoreduction (CC-0/1). Prognostic factors, cure rate and patterns of recurrence were investigated, comparing the two time periods (Group A vs Group B).

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Results

We registered a reduction of Grade 3–5 complications, from 18.2% in Group A to 8.5% in Group B. Overall and recurrence-free survivals were significantly higher for Group B patients ($p < 0.001$): median survival was 54 months and 5-year overall survival 39.8%. Completeness of cytoreduction, primary tumor histology and time period were independent prognostic factors. Median DFS was 16 months. A relapse was detected in 89% of patients with optimal cytoreduction. Main sites of relapse were peritoneum and distant metastases, mainly to liver and lungs. Peritoneal and liver/lung metastases presented as isolated recurrence in 73% and 58% of cases, respectively. As a consequence of updating of selection criteria, after 2004 we operated on significantly less patients with G3, T4, N positive or N2 primary. Furthermore, we mainly selected patients with PCI <16 (89% vs 54.5%, $p = 0.01$). Finally, we must underline that after 2004, preoperative chemotherapy was more extensively used (83% vs 50.0%, $p = 0.02$).

Conclusion

By a selection policy based on patient's features, disease extension and primary tumor factors, a median survival higher than 50 months can be expected. Most patients will eventually recur, mainly in the peritoneum. The pattern of recurrence suggests further investigation for more effective intraperitoneal therapies and repeated surgical treatments.

C21
HIPEC EXPERIENCE IN A RURAL COMMUNITY HOSPITAL USING MODIFIED PERFUSION SYSTEM

S. Saha, J. Edwards, A. Onitilo

Marshfield Clinic - Eau Claire (United States)

Objectives

Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) is a promising therapeutic modality in peritoneal carcinomatosis (PC) management. Pioneers of HIPEC have used modified perfusion devices. Present day commercial perfusion devices are expensive and are a limiting factor to provide HIPEC especially for smaller community hospitals.

Methods

Use of a modified perfusion pump for HIPEC was evaluated at the Marshfield Clinic, a multi-specialty tertiary care facility in rural Wisconsin, USA. Modification was made to a cardiac surgery perfusion pump by addition of a heater to achieve a temperature up to 45 Celcius (C). Internal quality control studies were performed prior to use of this device. The circuit consisted of a base console with centrifugal pump Bio-Medicus 550, a cardioplegia heat exchanger and a cardiotomy reservoir, all connected by 3/8-inch and ¼-inch polyvinyl chloride tubing (Medtronic Inc., Minneapolis, MN). Dianeal PD-2 (Baxter Healthcare, McGaw Park, IL) was used to prime the circuit.

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Results

Between January 2008–December 2011, 23 CRS and HIPEC procedures were done in 22 patients (11 male, 11 female) with PC in Marshfield Clinic, Marshfield, WI. Mean age was 55.3 years (39–73). PC Index was high in 10 patients, intermediate in 7, and low in 6. Highest inflow temperature was 45 degrees C, with most cases between 40–44 degrees C to achieve outflow/ intraperitoneal temperature between 40–42 degrees C. Average total perfusion time was 116 minutes (98–150). Average time to optimize intraperitoneal temperature was 22 minutes (10–70). Average drug perfusion time was 94 minutes (81–122). No patient died from the procedure, but major complication increasing hospital stay occurred in five patients (anastomotic leak, wound dehiscence, perineal cellulitis). As of Mar 31, 2018, 17 patients have died. Shortest survival was 6.7 months (primary peritoneal and gastric cancer) and longest is 116.7 months. 5 patients with papillary serous, colorectal and appendiceal carcinoma are alive with median follow up 43.7 months.

Conclusion

A single surgeon's data presented here shows that use of our modified perfusion pump has been, safe and effective, with comparable outcome. With resources and training, CRS and HIPEC for PC can be safely done in a rural community hospital.

C22

SYNCHRONOUS PERITONEAL METASTASES OF BREAST CANCER ORIGIN: A POPULATION-BASED STUDY ON INCIDENCE, RISK FACTORS AND SURVIVAL

M. Bushati[1], K.P. Rovers[2], L. De Munck[3], P.A.J. Vissers[3], S. Siesling[4], I.H.J.T. De Hingh[2]

[1]Department of Surgery, Oncology and Gastroenterology Unit, University of Padova - Padua (Italy), [2]Department of Surgery, Catharina Hospital, P.O. Box 1350, 5602 ZA - Eindhoven (Netherlands), [3]Department of Research, Netherlands Comprehensive Cancer Organisation (IKNL), P.O. Box 19079, 3501 DB - Utrecht (Netherlands), [4]Department of Health Technology and Services Research, Twente University - Enschede (Netherlands)

Objectives

Peritoneal metastases (PM) may arise from virtually all primary malignancies and are notorious for their detrimental impact on survival. Also breast cancer may metastasize to the peritoneum, but currently there is little knowledge on this phenomenon. The aim of this population-based study was to provide population based reliable data on the incidence, risk factors and prognosis of patients with PM of breast cancer origin.

Methods

All patients with a breast cancer diagnosis and distant metastases at first presentation (Stage IV), between 1989 and 2015, were selected from the Netherlands Cancer Registry. Incidence and survival were computed and risk factors for PM were determined using multivariable logistic regression analysis.

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Results

Of the 12,036 included patients diagnosed with metastatic breast carcinoma, 372 (3,1%) presented with synchronous PM. The only independent risk factor for presentation with synchronous PM was a lobular histology (Odds Ratio 6.38, 95% Confidence Interval 4.89–8.32). Median overall survival (OS) of patients with metastatic breast cancer was 23.5 months, but only 10.4 months for patients with PM (log-rank 0.17). OS of patients with PM was longer for lobular as compared to ductal carcinomas (24.3 vs 4.6 months, respectively; $p < 0.001$). However, this was fully attenuated when the cohort was restricted to hormone receptor-positive and HER2-negative tumors.

Conclusion

Synchronous PM occur in 3% of breast cancer patients with metastases at first presentation, especially in those with an invasive lobular carcinoma. Given the dismal impact of PM on survival, efforts should be undertaken to further develop effective therapies.

C23

SARCOPENIA IS A PREDICTIVE FACTOR ON MORBIDITY AND OVERALL SURVIVAL IN PATIENTS WITH COLORECTAL CANCER PERITONEAL METASTASIS

C. Agalar[1], S. Sokmen[1], N.C. Arslan[1], C. Altay[2], I. Basara[2], A.E. Canda[1], F. Obuz[2]

[1]Dokuz Eylul University School of Medicine, Department of General Surgery - Izmir (Turkey), [2]Dokuz Eylul University School of Medicine, Department of Radiology - Izmir (Turkey)

Objectives

Sarcopenia is defined as a decrease in muscle mass, strength, and function. Sarcopenia has been shown to be associated with the operative morbidity and mortality and the oncologic outcomes both in the elderly population and in patients with stomach, liver, pancreas, colorectal cancer.

The aim of this study is to investigate the role of the presence of sarcopenia on overall survival and morbidity in complex group of patients, who suffered from colorectal cancer peritoneal metastasis and underwent cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) at single center.

Methods

Patients demographics and oncological follow-up data were analyzed retrospectively from a prospectively collected database. Patients who underwent radically complete (CC-0, CC-1) CRS and HIPEC, and completed the follow-up were included to the study.

Total muscle volumes of the psoas muscles, paraspinal muscles and anterior abdominal wall muscles at L3 level in preoperative computerized tomography (CT) were calculated in the radiologic workstation. Patients having L3 skeletal muscle index below 52·4 cm^2/m^2 for men and 38·5 cm^2/m^2 for women were classified as sarcopenic.

Patients who underwent incomplete cytoreduction (CC-2), died in early perioperative period and patients having L3 level abdominal wall defect or stoma were not included into the study.

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Results

Sixty-five patients (42 women, 23 men) enrolled to the study, median age was 54.4 ± 13.4 (22–86) years. 20 patients (30.8%) were defined as sarcopenic (14 women, 6 men; Chi-square; p = 0.588)

The morbidity was observed in 30 patients (46.2%); morbidity rates was 70% in sarcopenic group and 35.5% in non-sarcopenic group (Chi-square; p = 0.015).

Median follow-up time was 33.28 ± 21.9 (3.6–95.2) months. The median overall survival of sarcopenic and non-sarcopenic group were 24.53 ± 3.6 and 53.64 ± 5.6 months, respectively (log-rank; p = 0.005).

Conclusion

Sarcopenia assessed with preoperative CT is a robust, easily applied, and cost-effective confidential predictive factor on morbidity and overall survival in patients with colorectal peritoneal metastasis.

C24

ARTIFICIAL NEURAL NETWORKS TO PREDICT OUTCOMES AFTER CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY: A TOOL FOR PATIENTS SELECTION

M. Prodeau[1], V. Kepenekian[2], F. Mercier[2], F.R. Pruvot[1], P. Zerbib[1], O. Glehen[2], G. Passot[2]

[1]CHRU Lille - Lille (France), [2]CHU Lyon Sud - Lyon (France)

Objectives

Expected morbidity and early recurrence are the 2 main parameters to select patients with peritoneal carcinomatosis (PC) for potentially curative cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS+HIPEC). Models based on artificial neural networks (ANN) could predict outcomes after surgery. To determine ANN to predict the post-operative morbidity and early recurrence after CRS+HIPEC with only variables available before resection.

Methods

From the institutional prospective HIPEC database, all patients who underwent complete cytoreductive surgery for PC from non-gynecologic origin (colorectal, peritonei pseudomyxoma, malignant peritoneal mesothelioma and gastric) between January 2008 and December 2015 were extracted. Postoperative morbidity was graded at 90 day using Dindo-Clavien classification. Recurrence was evaluated 6 months after CRS+HIPEC. Preoperative variables and preoperative variables available before surgery were used. Multiple imputation method was used to deal with missing data (15%). An ANN for postoperative morbidity and for recurrence were constructed. ANN is a novel machine learning method inspired by the biological neural networks that constitute animal brains. Variable was selected for ANN if it was statistically associated with end-point on univariate analysis ($p < 0.05$). For post-operative morbidity and recurrence, accuracy and correlation's coefficient were respectively calculated.

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Results

Among 504 patients included, the origin of peritoneal carcinomatosis was colorectal, peritonei pseudomyxoma, malignant peritoneal mesothelioma and gastric for 276, 132, 55, and 41 patients, respectively. The PCI mean was 11.5. A postoperative complication occurred for 151 patients (30.0%). The 90-days mortality was 2.8%. At 6 months, 68 patients presented with recurrence (14%). For post-operative mortality 7 variables were included: gender, PCI, albumin, anastomosis number, splenectomy, glissonectomy, pelvis surgery. For recurrence, 5 variables were used: gender, PC origin, PCI, HIPEC and albumin. Accuracy was 0.65 for post-operative morbidity and correlation's coefficient was 0.84 for recurrence.

Conclusion

By accurately predicting the risk of post-operative morbidity and recurrence at 6 months, the 2 ANN should be useful at patient's selection after complete surgical exploration and before surgical resections.

C25

MULTIDISCIPLINARY TREATMENT COMBINING GASTRECTOMY WITH INTRAPERITONEAL AND SYSTEMIC CHEMOTHERAPY FOR GASTRIC CANCER WITH PERITONEAL METASTASIS: A SINGLE CENTER EXPERIENCE OVER 10 YEARS

H. Ishigami[1], H. Yamaguchi[2], H. Yamashita[1], M. Asakage[3], J. Kitayama[2]

[1]The University of Tokyo - Tokyo (Japan), [2]Jichi Medical University - Tochigi (Japan), [3]Hitotsubashi Hospital - Tokyo (Japan)

Objectives

The standard of care for gastric cancer with distant metastasis is systemic chemotherapy. Systemic chemotherapy has made remarkable progress recently, but the prognosis of gastric cancer patients with peritoneal metastasis (P1) or positive peritoneal cytology (CY1) remains poor. We developed several regimens combining intraperitoneal (IP) taxanes and systemic chemotherapy, and evaluated the safety and efficacy in clinical trials. Moreover, gastrectomy after response to IP and systemic chemotherapy is a promising option for P1 or CY1 gastric cancer. A single-institution retrospective study was performed to evaluate the efficacy and safety of this multidisciplinary treatment strategy.

Methods

This study enrolled 158 primary P1 or CY1 gastric cancer patients treated with long-term IP paclitaxel or docetaxel and systemic chemotherapy at the University of Tokyo Hospital between 2005 and 2015. Gastrectomy was performed when peritoneal cytology reverted to negative, and the disappearance or marked shrinkage of peritoneal metastasis was confirmed by second-look laparoscopy. Combination chemotherapy was restarted after surgery and repeated with appropriate modification.

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Results

Gastrectomy was performed in 94 (P1 85, P0CY1 9) of 158 (P1 147, P0CY1 11) patients after response to chemotherapy. Curative (R0) resection was achieved in 61 of 94 patients (65%). Histological response of grade Ib or higher (viable tumor cells ≤2/3) was obtained in 44 patients (47%). Postoperative complications included anastomotic leakage in 3 patients and pancreatic fistula in 2 patients, which were cured conservatively. The median survival time (MST) of 94 patients with gastrectomy was 31.3 months (95% confidence interval [CI] 26.1–39.3 months). Relapse or progression was observed in 78 of 94 patients with a median time of 17.9 months (95% CI 15.0–24.2 months). The MST of 64 patients without gastrectomy was 12.3 months (95% CI 10.0–13.9 months). There were no treatment-related deaths.

Conclusion

Multidisciplinary treatment combining gastrectomy with IP and systemic chemotherapy is safe and may prolong the survival of P1 and CY1 gastric cancer patients.

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GASTRECTOMY AFTER INTRAPERITONEAL PLUS SYSTEMIC CHEMOTHERAPY FOR GASTRIC CANCER PATIENTS WITH PERITONEAL METASTASIS OR POSITIVE PERITONEAL CYTOLOGY: ANALYSIS OF 124 PATIENTS FROM FOUR CLINICAL TRIALS

M. Aizawa[1], H. Ishigami[2], T. Omori[3], Y. Kodera[4], R. Fukushima[5], M. Imano[6], T. Arigami[7], T. Tomita[8], K. Kishi[9], T. Matsumura[10], Y. Ito[11], Y. Hirono[12], Y. H[1], H. Yamaguchi[13], J. Kitayama[13]

[1]Niigata Cancer Center Hospital - Niigata (Japan), [2]The University of Tokyo - Tokyo (Japan), [3]Osaka International Cancer Institute - Osaka (Japan), [4]Nagoya University - Nagoya (Japan), [5]Teikyo University - Tokyo (Japan), [6]Kindai University - Osakasayama (Japan), [7]Kagoshima University - Kagoshima (Japan), [8]Hyogo College of Medicine - Nishinomiya (Japan), [9]Osaka Police Hospital - Osaka (Japan), [10]Aichi Medical University - Nagakute (Japan), [11]Aichi Cancer Center Hospital - Nagoya (Japan), [12]University of Fukui - Fukui (Japan), [13]Jichi Medical University - Shimotsuke (Japan)

Objectives

The prognosis of gastric cancer patients with peritoneal metastasis (P1) or positive peritoneal cytology (CY1) remains dismal, with a median survival time (MST) of around or less than one year by standard systemic chemotherapy. Intraperitoneal (IP) chemotherapy with taxanes has local effects due to high concentrations in the peritoneal cavity. Multidisciplinary treatment combining surgery with IP plus systemic chemotherapy is a promising option for P1 or CY1 gastric cancer.

Methods

We evaluated the safety and efficacy of surgery in four clinical trials of chemotherapy regimens, three regimens (S-1/paclitaxel [PTX]+IP PTX, S-1/oxaliplatin+IP PTX, capecitabine/cisplatin+IP docetaxel) in P1 patients and one regimen (S-1/PTX+IP PTX) in P0CY1 patients. In these trials, gastrectomy was recommended when the disappearance or marked shrinkage of peritoneal metastasis was confirmed by second-look laparoscopy. Combination chemotherapy was restarted after surgery and repeated with appropriate modification.

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Results

Gastrectomy was performed in 124 (P1 93, P0CY1 31) of 260 (P1 222, P0CY1 38) patients after response to chemotherapy. Fifty-seven of 124 patients had malignant ascites. The mean peritoneal cancer index was 9.4 (SD 9.7) in 93 P1 patients. Total and distal gastrectomy were performed in 100 and 24 patients, respectively. Curative (R0) resection was achieved in 80 patients (65%). Histological response of grade Ib or higher (viable tumor cells ≤2/3) was obtained in 55 patients (44%). The MSTs of P0CY1 and P1 patients were 31.0 months (95% confidence interval [CI] 25.7 months–not reached) and 26.3 months (95% CI 21.3–34.2 months), respectively. The median relapse or progression free survival of P0CY1 and P1 patients were 27.2 months (95% CI 19.5–not reached) and 19.0 months (95% CI 13.9–25.8 months), respectively. Postoperative complications of Clavien-Dindo grade II–IVa occurred in 11 patients (9%). There were no treatment-related deaths.

Conclusion

Gastrectomy for responders to IP plus systemic chemotherapy is safe and may prolong the survival in P1 or CY1 gastric cancer patients.

C27

CYTOREDUCTIVE SURGERY & HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR SYNCHRONOUS VERSUS METACHRONOUS COLORECTAL PERITONEAL METASTASES

J. Wong, G. Tan, W.Y. Ng, C. Chia, M. Teo

National Cancer Centre Singapore - Singapore (Singapore)

Objectives

Colorectal peritoneal metastases (CPM) occur in up to 13% of patients with colorectal cancer, presenting either synchronously or metachronously. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) have been increasingly utilized for selected patients with CPM with favorable outcomes but the benefits of such therapy may be more pronounced in one group over another. Our study aims to compare the results of CRS and HIPEC for synchronous (s-CPM) versus metachronous CPM (m-CPM).

Methods

A retrospective analysis of prospectively collected data of patients with s-CPM and m-CPM treated with CRS and HIPEC at the National Cancer Centre Singapore between January 2003 to January 2018 was performed. In the s-CPM group, CRS & HIPEC was performed at the time of primary tumor resection or within 6 months from primary surgery. In the m-CPM group, patients had developed isolated peritoneal metastases >6 months after primary curative surgery and underwent CRS & HIPEC thereafter. Patient, tumor characteristics, extent of peritoneal disease as measured by the peritoneal carcinomatosis index (PCI) and survival outcomes were compared.

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Results

103 patients with CPM were treated with CRS and HIPEC during the study period; 20 (19.4%) patients had s-CPM and 83 (80.6%) had m-CPM. Majority of patients (91%, n = 94) had T3 or T4 primary tumors. 95% received either chemotherapy or chemoradiation therapy prior to CRS & HIPEC. Complete CRS (CC score = 0/1) was achieved in 99% of patients. The median PCI was 9 (range 3–27) in the s-CPM group and 6 (range 0–27) in m-CPM.

Recurrences occurred in 45% (n = 9/20) of s-CPM and in 54% (n = 45/83) of m-CPM (p = 0.619), with the disease free interval (DFI) of 17.5 vs 38.5 months (p = 0.006) for s-CPM vs. m-CPM. However, there was no difference in the disease-free survival (DFS) between the groups (p = 0.642). The median overall survival (OS) was 26.9 vs 43.5 months in the s-CPM and m-CPM groups respectively, and 1- 3- and 5-yr OS was 77.0%, 27.5% and 13.8 in s-CPM vs 91.2%, 61.7% and 31% in m-CPM (p = 0.037).

Conclusion

Patients with s-CPM undergoing CRS and HIPEC tend to recur earlier, and have a poorer OS when compared with CPM patients who present metachronously. This likely represents differences in disease biology and further prospective studies are needed to determine the appropriate management of s-CPM versus m-CPM.

C28

RESULTS OF DIFFERENT TREATMENT OPTIONS FOR PATIENTS WITH GASTRIC CANCER WITH PERITONEAL METASTASES IN 100 CONSECUTIVE PATIENTS – A SINGLE CENTER EXPERIENCE

A. Brand[1], P. Thuss-Patience[2], W. Raue[3], J. Hartmann[3], M. Biebl[1], J. Pratschke[1], B. Rau[1]

[1]Department of Surgery, Campus Virchow-Klinikum and Charité Campus Mitte, Charité - Universitätsmedizin Berlin, Berlin, Germany - Berlin (Germany), [2]Department of Hematology and Oncology, Division of Palliative Medicine, Campus Virchow, Charité, Universitätsmedizin Berlin, Berlin, Germany - Berlin (Germany), [3]Department of General, Visceral and Thoracic Surgery, AKH Celle, Celle, Germany - Berlin (Germany)

Objectives

Patients with peritoneal metastases of gastric cancer have a poor prognosis with a median survival of 7 months. The aim of this study was to explore and compare several treatment options and their outcome based on the Peritoneal Cancer Index (PCI) during the past 9 years.

Methods

This retrospective analysis included between 11/2005 and 12/2016 patients with gastric cancer and peritoneal metastases diagnosed and proven by laparoscopy. Three groups were analyzed: 1) CRS & HIPEC in combination with systemic chemotherapy (n = 63), 2) tumor debulking & HIPEC in combination with systemic chemotherapy (n = 14) and 3) systemic chemotherapy only (n = 23). Tumor debulking was performed in case the primary tumor could not be removed with free tumor margins (R0).

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Results

A total of 100 patients with an age of 53.19 ± 11.2 years with a PCI of 15.3 ± 11.8 were included. The PCI in group 1 (9.2 ± 7.2) was significantly lower than in group 2 (27.1 ± 9.8, $p < 0.001$) and group 3 (24.8 ± 11.3; $p < 0.001$). Mean time from diagnosis to laparoscopy was 6.0 ± 6.3 months. Patient´s median overall survival was 10.4 ± 0.8 for group 1, 6.3 ± 0.6 for group 2 and 5.9 ± 1.4 months for group 3 ($p < 0.001$), respectively. Significant predictors for survival of the full cohort was PCI (HR 1.03; $p = 0.001$) and completeness of cytoreduction (HR 2.44; $p = 0.02$) in patients treated with CRS & HIPEC. Tumor regression grade (Becker) 1 showed better median survival compared to grade 2 and 3 (60.5 vs. 10.8 vs. 8.0 months).

Conclusion

CRS & HIPEC showed convincing results in selected patients. Tumor debulking in combination with HIPEC showed no improvement of median survival compared to systemic chemotherapy only. Further studies are needed to evaluate tumor regression grade as criteria for patient selection in CRS & HIPEC.

C29

THE USE OF SMALL BOWEL PCI SCORE AS A PROGNOSTIC INDEX IN PATIENTS WITH PERITONEAL CARCINOMATOSIS SECONDARY TO COLORECTAL CANCER

J. Spiliotis[1], V. Kalles[1], I. Kyriazanos[1], N. Kopanakis[2], A. Terra[2], E. Efstathiou[2], A. Prodromidou[2], A. Christopoulou[3]

[1]Peritoneal Surface Oncology, Athens Medical Group - Athens (Greece), [2]Department of Surgery, Metaxa Anticancer Hospital - Piraeus (Greece), [3]Department of Oncology, S. Andreas General Hospital of Patras - Patras (Greece)

Objectives

Peritoneal carcinomatosis (PC) from colorectal cancer has a very poor prognosis and is relatively resistant to systemic chemotherapy. In selected patients, the combination of extensive cytoreductive surgery in with hyperthermic intra-operative intraperitoneal chemotherapy (HIPEC) can confer a benefit in survival. Traditionally, the disease burden has been evaluated using the Peritoneal Cancer Index (PCI) score. The present study aims to evaluate the small bowel subset of the PCI (SB-PCI) score as a prognostic factor in patients with PC secondary to colorectal cancer.

Methods

A retrospective analysis of patients that underwent cytoreduction and HIPEC for recurrent colorectal cancer with PC between 2010–2017 was performed. For each case, patient characteristics, procedure details, and clinical outcomes were recorded. Intraoperatively, both the PCI score and the SB - PCI score were documented. The statistical analysis was performed using the SPSS v21.0 statistical package.

Results

80 patients (44 males–36 females) with a mean age of 57 years (range 33–75) years were included in the analysis. The mean intraoperative PCI score was 16,8 (range 1–39) with a mean small bowel PCI score of 5,9 (range 0–12). The mean operative time was 241 minutes (140–510 minutes). CC0/1 was achieved in 62/80 patients (77,5%). 30/80 patients (37,5%) required postoperative ICU admission and the mean length of postoperative stay was 11,6 days. Severe complications (Clavien – Dindo III/IV) were encountered in 20% of the cases whereas the 30-day mortality rate was 2,5%. The mean follow – up period was 26,3 months.

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Univariate regression analysis showed that the PCI score (OR 1,18), the SB – PCI score (OR 1,4) and the CC score correlated significantly with overall survival. When entered in a multivariate regression model, only the SB – PCI and the CC score correlated significantly with overall survival. Finally, when the SB – PCI was stratified in three groups (0–4, 5–8 and 9–12), Kaplan – Meier curve analysis showed a statistically significant difference in survival between the three groups.

Conclusion

Our results indicate that the SB – PCI correlates with overall survival in patients with peritoneal metastases secondary to colorectal cancer, and its use should be further investigated in larger patient series.

C30

ANALYSIS OF RE-HIPEC FOR RECURRENT PERITONEAL CARCINOMATOSIS CONFINED TO THE ABDOMINAL WALL

E. Boldo, E. Fernandez, A. Mayol, R. Lozoya, S. Jareño, J.C. Pastor, A. Coret, D. Escribano, C. Martinez, C. Dehevia, C. Fortea, G. Perez De Lucia

CONSORCIO HOSPITALARIO PROVINCIAL CASTELLON - Castellon (Spain)

Objectives

Re-cytoreductive surgery (reCS) and repeat HIPEC (reHIPEC) is feasible and yields an accepted survival in highly selected peritoneal carcinomatosis (PC) patients. The aim of this study was to analyze characteristics and results of reHIPEC in the subgroup of patients with recurrent PC confined to the abdominal wall.

Methods

Thirty-two (32) colo-rectal cancer carcinomatosis patients were subjected to primary CS+HIPEC. Eligibility criteria for the analysis included: limited extent of the recurrent peritoneal disease (PCI < 20), exclusive abdominal wall PC location and reCRS+reHIPEC. Patient characteristics, primary and secondary PCI and CC, type of IP and adjuvant chemotherapy, postoperative complications and survival were recorded.

Results

From this series, three (1F:2M) patients were included. Most carcinomatosis were originated from T4 (2/3) tumors located at sigmoid colon (2/3). Median primary PCI was 4 and secondary 3. Relapses were located in areas that primary HIPEC could not reach (1 at medial periteneum and 2 at tube orifice). All patients resulted CC0 and received primary adjuvant IV chemotherapy. None received secondary IV adjuvant chemotherapy. Postoperative mortality (both after primary HIPEC and reHIPEC) was 0% and postoperative complications were grade 1–2. Mean primary peritoneal DFS was 16.3 months and secondary 15.5. One patient developed pulmonary metastasis 11 months after reHIPEC.

Conclusion

In our experience, reHIPEC in the subgroup of patients with recurrent PC confined to the abdominal wall achieve similar results to primary HIPEC. Our analysis suggests that medial peritonectomy and resection of the tube orifices at primary HIPEC would be preventive maneuvers for recurrent carcinomatosis.

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C31
CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR PERITONEAL MALIGNANCIES AT THE NATIONAL CANCER CENTRE SINGAPORE

G. Tan, C. Chia, W.Y. Ng, J. Ong, K.C. Soo, M. Teo

National Cancer Centre Singapore - Singapore (Singapore)

Objectives

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) are increasingly being utilised in the treatment of peritoneal malignancies. We provide a review of a high-volume Asian institute's experience and outcomes with this procedure.

Methods

Data were prospectively collected from 300 consecutive CRS and HIPEC procedures performed at the National Cancer Centre Singapore between April 2001 and December 2017. Our primary endpoints were overall survival (OS) and disease-free survival (DFS), and secondary endpoints were morbidity and mortality.

Results

77.3% of patients were Chinese, 3.7% were Malay, 4.3% were Indian and 14.7% were of other ethnicities. Primary tumours were colorectal (34.7%), ovarian and primary peritoneal (31.6%), appendiceal (23.7%), mesothelioma (4.3%) and others (5.7%). The median peritoneal cancer index was 10, and 87.2% of patients achieved a completeness of cytoreduction score of 0/1. High-grade morbidity occurred in 19.7% of cases, and there were no 30-day mortalities. At 5-years, the OS was 47.6% and DFS was 24.4%. The only factor associated with improved OS on multivariate analysis was the PCI score ($p = 0.034$).

Conclusion

The combined treatment of CRS and HIPEC is beneficial and associated with reasonable morbidity and mortality in Asian patients with peritoneal disease from colorectal, ovarian, appendiceal, primary peritoneal and mesothelioma primaries. The extent of peritoneal disease is the most important prognostic factor for survival.

C32
ANALYSIS OF MORBIDITY ASSOCIATED WITH ABDOMINAL WALL RESECTION AND RECONSTRUCTION AFTER CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (CRS/HIPEC)

R. Parikh[1], S. Shah[2], V. Dhurandhar[3], N. Alzahrani[1], D. Morris[1]

[1]Hepatobiliary and Surgical Oncology Unit, Department of Surgery, St George Hospital, Kogarah - Sydney, NSW (Australia), [2]Seth G.S. Medical College, King Edward VII Memorial Hospital, Parel - Mumbai (India), [3]Royal Prince Alfred Hospital - Sydney, NSW (Australia)

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Objectives

Cytoreductive surgery and Heated Intraperitoneal Chemotherapy (CRS/HIPEC) has evolved as an effective method for the management of selected patients with peritoneal metastatic disease. It is often associated with abdominal wall resection (AWR) to achieve complete cytoreduction (CC), especially in patients with a high peritoneal carcinomatosis index (PCI). This often requires complex reconstructions leading to wound complications (WC), wound dehiscence (WD) and a delay in post-operative chemotherapy. The aim of our study is to analyze factors associated with poor outcomes post AWR and those associated with wound recurrence.

Methods

A review of a prospective database of 1074 patients undergoing CRS/ HIPEC procedures from 1996 to 2017 at St. George Hospital revealed 197 patients who underwent AWR. Tumour types included appendix, colon, rectum, ovarian, mesothelioma and Disseminated Peritoneal Adenomucinosis.

Results

AWR and reconstruction for proven or suspected abdominal wall and wound/port site metastases was performed in 197 (18.3%) patients. PCI ≥ 20 found in 45 (22.8%), CC (0–1) achieved in 192 (97.4%). Mean length of surgery was 479 min and 160 (81.2%) had preoperative albumin ≥ 3.5g/L. Grade III WC (Clavien-Dindo's Classification) were found in 21 (10.6%). WD was found in 14 (7.1%) compared to 30 (3.4%) in 877 patients without AWR (OR 2.07, CI 1.08–3.99, p = 0.028). Primary fascial closure was performed in 115 (58.4%), biological mesh repair in 34 (17.3%), synthetic mesh repair in 26 (13.1%) and component separation technique (CST) with or without mesh repair in 21 (10.6%) patients compared to 841 (95.9%), 10 (1.14%), 17 (1.9%) and 7 (0.79%) respectively in patients without AWR. Midline wound recurrence was seen in 26 (13.3%) with a mean time to recurrence of 18 months. Multivariate regression analysis showed that age (OR 1.06, CI 1.01–1.11, p = 0.022) and CST (OR 9.63, CI 2.55–36.23, p = 0.001) were significant predictors of Grade III WC, and CST (OR 4.19, CI 1.27–13.86, p = 0.019) was a significant predictor of WD. The presence of a higher prior surgical score (PSS) 2–3 (2.74, CI 1.16–6.49, p = 0.022) was a significant predictor of midline WR.

Conclusion

The results of this study demonstrate that patients undergoing AWR were associated with higher incidence of postoperative WD. CST was associated with an increased incidence of Grade III WC and WD. Patients with a higher PSS had a significantly higher incidence of midline wound recurrence.

C33

INTRAOPERATIVE PACKED RED BLOOD CELL TRANSFUSION (IPRBT) AND IPRBT TO PCI RATIO NEGATIVELY AFFECT OUTCOMES OF PATIENTS UNDERGOING CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY – AN ANALYSIS OF 880 PATIENTS

O.M. Fisher, N. Alzahrani, M. Kozman, A. Mohammad, S. Valle, W. Liauw, D. Morris

Liver & Peritonectomy Unit, St George Hospital - Sydney (Australia)

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Objectives

To investigate the relationship of intraoperative packed red blood cell transfusion (iPRBT) and the iPRBT to peritoneal cancer index (PCI) ratio with outcomes of patients undergoing cytoreductive surgery (CRS) and heated intraoperative chemotherapy (HIPEC).

Methods

A retrospective analysis of the St George Hospital CRS/HIPEC database. The relationship between amount iPRBT and PCI was determined through regression analysis. Further, each patient's iPRBT to PCI ratio was calculated to generate a normalised intra-patient index variable of blood product usage per volume of disease. The impact hereof on short and long term outcomes was analysed.

Results

880 patients were included for analysis. Patients with higher PCIs required more iPRBT ($p < 0.001$). An increased iPRBT/PCI ratio resulted in more Clavien-Dindo Grade III/IV complications (52.2% vs. 30.9%, $p<0.001$) and consequently longer hospital length of stay. An increased iPRBT/PCI ratio was associated with worse median overall (OS) and recurrence free survival (103 vs. 42 and 30 vs. 13 months, both $p < 0.001$). Furthermore, we found that any exposure to iPRBT conferred a negative survival impact. Conversely, in colorectal cancer patients a dose-response effect was seen, where incremental iPRBT requirements resulted in diminished survival times. In a multivariable Cox proportional hazards model that corrected for potential confounders an increased iPRBT/PCI ratio was an independent predictor of worse OS (aHR 2.08, 95%CI 1.57–2.77, $p < 0.001$).

Conclusion

Increased iPRBT and an elevated iPRBT/PCI ratio severely impact short and long-term outcomes of CRS/HIPEC patients. Attempts at identifying patients at highest risk of iPRBT and preoperative optimisation of risk factors is pertinent to improving outcomes of patients undergoing CRS/HIPEC.

C34

THE IMPACT OF GASTRECTOMIES ON PATIENTS REQUIRING CYTOREDUCTIVE SURGERY AND HEATED INTRAPERITONEAL CHEMOTHERAPY FOR ADVANCED LOWER GASTROINTESTINAL MALIGNANCIES – A PROPENSITY-SCORE MATCHED ANALYSIS

O.M. Fisher, J. Lansom, M. Kozman, M. Alshahrani, S. Valle, N. Alzahrani, W. Liauw, D. Morris

Liver & Peritonectomy Unit, St George Hospital - Sydney (Australia)

Objectives

To investigate outcomes of patients with lower gastrointestinal cancer requiring gastrectomy to achieve complete resection during cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC).

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Methods

Colorectal and appendiceal cancer patients requiring partial or complete gastrectomy were identified from the St George CRS/HIPEC database. Complications & survival outcomes were compared between gastrectomy vs. nongastrectomy groups. Propensity score matching was performed for adjustment of patient factors.

Results

68/718 patients (9.5%) required partial/wedge (n = 12), distal (n = 46), subtotal (n = 9) or total (n = 1) gastrectomy. Before matching, patients requiring any type of gastrectomy had higher grade III/IV complication (73.5 vs 38.6% $p < 0.001$) & increased in-hospital mortality rates (5.8 vs 0.9% $p = 0.009$). Further, gastrectomy reduced median overall and recurrence free survival (37 vs 70 & 16 vs 20 months $p < 0.001$ & $p = 0.005$). However, following propensity score matching for age, histopathology, signet ring cell status, preoperative tumour marker levels, preoperative nutritional status, ASA score, PCI, completeness of cytoreduction, procedure duration, and intraoperative packed red blood cell requirements, the previously identified survival difference disappeared (69 vs 37 months, $p = 0.06$), but differences in major complication remained (74% vs 58%, $p = 0.04$) whilst in-hospital mortality rates equalized.

Conclusion

Previously identified differences in outcomes of patients requiring gastrectomy during CRS/HIPEC may be an artifact of underlying confounding factors. Thus, gastrectomy remains an essential aspect CRS/HIPEC for advanced lower-GI malignancies, although the morbidity of the procedure should be considered during pre- and intraoperative decision making.

C35

SOFT TUMOUR CONSISTENCY AND USE OF 5-FU EPIC ARE BOTH ASSOCIATED WITH IMPROVED SURVIVAL IN APPENDICEAL ADENOCARCINOMA FOLLOWING CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY SHORT TITLE: TUMOUR TEXTURE AND APPENDIX CANCER

Y. Huang[1], N. Alzahrani[2], O. Fisher[1], T. Chua[3], M. Kozman[1], W. Liauw[4], A. Arief[5], S. Valle[1], D. Morris[1]

[1]Department of Surgery, St George Hospital, New South Wales, University of New South Wales, Australia - Sydney (Australia), [2]Department of Surgery, St George Hospital, New South Wales, University of New South Wales, Australia; College of Medicine, Al Imam Muhammad Ibn Saud Islamic University (IMSIU), Riyadh, Saudi Arabia - Sydney (Australia), [3]Department of Gastrointestinal Surgery, Royal North Shore Hospital, St Leonards, NSW, Australia - Sydney (Australia), [4]Department of Medical Oncology, St George Hospital, New South Wales, University of New South Wales, Australia - Sydney (Australia), [5]College of Medicine, Al Imam Muhammad Ibn Saud Islamic University (IMSIU), Riyadh, Saudi Arabia - Sydney (Australia)

Objectives

It has been increasingly recognised that appendiceal adenocarcinoma with peritoneal metastases is not a homogenous disease. The aim of this study was to examine the impact of intraoperative macroscopic tumour hardness on short-term operative outcomes and long-term overall survival in appendiceal adenocarcinoma.

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Methods

This was a retrospective study of prospectively collected data of patients with appendiceal adenocarcinoma treated by cytoreductive surgery and intraperitoneal chemotherapy. Group I included patients with macroscopically soft tumour, defined as peritoneal gelatinous tumours that are soft and jelly-like; Group II included those with macroscopically hard tumour nodules without gelatinous features; Group III included those with both soft and hard features. Subgroup analysis was performed on use of EPIC.

Results

A total of 526 patients were diagnosed with an appendiceal mucinous neoplasm with peritoneal dissemination during the study period. 192 patients were included in this study. The three groups had similar hospital mortality, mean intensive care unit, high dependency unit and total hospital stay. Patients with soft tumours had significantly longer 1-, 3- and 5-year overall survival rates compared to other groups (soft tumours: 96.5%, 83.5%, and 62.0% vs. hard tumours: 79.0%, 45.7%, and 32.3% vs. intermediate tumours: 84.7%, 67.3%, and 49.1%, $p < 0.001$). Equally, median disease-free survival was significantly better in soft tumours. Multivariable analysis identified tumour hardness as an independent prognostic marker (HR for hard tumours = 4.43, 95%CI 2.19–9.00), after adjusting for potentially confounding factors.

Conclusion

Patients with macroscopically soft tumours showed an improved OS. Intraoperative macroscopic tumour hardness may potentially be used as a prognostic marker for long-term survival. Additionally, the use of EPIC might be beneficial in patients with appendiceal adenocarcinoma, especially those with soft mucins.

C36

EARLY POSTOPERATIVE INTRAPERITONEAL CHEMOTHERAPY IS ASSOCIATED WITH SURVIVAL BENEFIT FOR APPENDICEAL ADENOCARCINOMA WITH PERITONEAL DISSEMINATION

D. Morris[1], Y. Huang[1], N. Alzahrani[2], W. Liauw[3]

[1]Department of Surgery, St George Hospital, New South Wales, University of New South Wales, Australia - Sydney (Australia), [2]Department of Surgery, St George Hospital, New South Wales, University of New South Wales, Australia; College of Medicine, Al Imam Muhammad Ibn Saud Islamic University (IMSIU), Riyadh, Saudi Arabia - Sydney (Australia), [3]Department of Medical Oncology, St George Hospital, New South Wales, University of New South Wales, Australia - Sydney (Australia)

Objectives

The combined approach of cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) has achieved encouraging outcomes for patients with PMCA with peritoneal dissemination. However, there is little evidence for the use of early postoperative intraperitoneal chemotherapy (EPIC) in addition to HIPEC in this group of patients. This study aims to assess the short-term and long-term outcomes of use of EPIC in a large cohort of patients with PMCA uniformly treated by CRS and PIC, all of whom received HIPEC and most of whom also received EPIC.

Methods

This was a retrospective study of prospectively collected data of consecutive patients with PMCA who underwent CRS and perioperative intraperitoneal chemotherapy by one surgical team at St George Hospital in Sydney, Australia between Jan 1996 and Aug 2016.

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Results

A total of 185 patients formed the cohort of this study. However, there was no significant difference in terms of hospital mortality (p = 0.632), major morbidity rate (i.e. Grade III/IV) (p = 0.444), intensive unit care stay (p = 0.638) and total hospital stay (p = 0.0.078). However, patients who received HIPEC and EPIC had a significant longer stay in high dependency unit (p < 0.001). Multivariate analysis showed combined HIPEC with EPIC is an independent prognostic factor for better overall survival (Hazard ratio (HR) = 0.42, 95% confidence interval (CI) = 0.19–0.92, p = 0.030) and disease free survival (HR = 0.66, 95%CI = 0.44–0.99, p = 0.045), adjusted for age, sex, peritoneal cancer index, completeness of cytoreduction score, CEA ≥ 6.5 mg/L, CA19–9 ≥ 24.0 U/mL and CA125 ≥ 32.0 U/mL.

Conclusion

In summary, the combination of HIPEC and EPIC could potentially provide additional survival benefit for patients with PMCA with peritoneal spread as compared to HIPEC alone without increasing postoperative morbidity and mortality. Multi-institutional studies are warranted to further confirm the potential benefits of EPIC in PMCA and address the question of optimal drug and/or duration of EPIC.

C37

EARLY POSTOPERATIVE INTRAPERITONEAL CHEMOTHERAPY FOR LOW-GRADE APPENDICEAL MUCINOUS NEOPLASMS WITH PSEUDOMYXOMA PERITONEI- IS IT BENEFICIAL?

Y. Huang[1], N. Alzahrani[2], W. Liauw[3], D. Morris[1]

[1]Department of Surgery, St George Hospital, New South Wales, University of New South Wales, Australia - Sydney (Australia), [2]Department of Surgery, St George Hospital, New South Wales, University of New South Wales, Australia; College of Medicine, Al Imam Muhammad Ibn Saud Islamic University (IMSIU), Riyadh, Saudi Arabia - Sydney (Australia), [3]Department of Medical Oncology, St George Hospital, New South Wales, University of New South Wales, Australia - Sydney (Australia)

Objectives

There is little evidence for the use of EPIC in patients with low-grade mucinous neoplasms (LAMN) with pseudomyxoma peritonei (PMP). This study aims to assess the outcomes of use of EPIC in a large cohort of patients with LAMNs with PMP uniformly treated by CRS and PIC, all of whom received HIPEC and most of whom also received EPIC.

Methods

This was a retrospective study of prospectively collected data of consecutive patients with PC of appendix origin who underwent CRS and PIC by one surgical team at St George Hospital in Sydney, Australia between Jan 1996 and Nov 2015. Subgroup analyses were performed for patients with a high peritoneal cancer index >20 and also based on histopathological subtypes of LAMN.

Results

A total of 250 patients formed the cohort of this study. However there was no significant difference in terms of hospital mortality (p = 0.153), major morbidity rate (i.e. Grade III/IV) (p = 0.593), intensive unit care stay (p = 0.764) and total hospital stay (p = 0.927). However, patients who received HIPEC and EPIC had a significant longer stay in high dependency unit. Multivariate analysis showed combined HIPEC with EPIC is

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an independent prognostic factor for better survival outcomes (HR = 0.30, 95%CI = 0.12–0.74, p = 0.009), adjusted for age, PCI and histopathological subtypes.

Conclusion

In summary, the combination of HIPEC and EPIC can provide additional survival benefits for patients with LAMNs with PMP as compared to HIPEC alone without increasing postoperative morbidity and mortality. EPIC should be considered following CRS and HIPEC for patients with LAMNs with PMP.

C38

WHAT IS THE CLINICAL IMPACT OF NODAL STATUS ON SURVIVAL AFTER COMPLETE CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR PATIENTS WITH GASTRIC PERITONEAL METASTASIS?

P.E. Bonnot[1], D. Vaudoyer[1], F. Mercier[2], K. Abboud[3], L. Villeneuve[4], J.M. Bereder[5], F. Quenet[6], D. Goere[7], P. Meeus[8], S. Msika[9], C. Arvieux[10], J. Lefevre[11], D. Pezet[12], R. Wernert[13], P. Rat[14], N. Pirro[15], T. Courvoisier[16], R. Kianmanesh[17], F. Marchal[18], M. Pocard[19], O. Glehen[1]

[1]HCL, Centre Hospitalier Lyon Sud, Digestive and Oncological Surgery - Lyon (France), [2]CHUM Hospital Notre-Damem Surgical Oncology - Montreal (Canada), [3]CHU Saint Etienne, Digestive and Oncological Surgery - Saint Etienne (France), [4]HCL,Unité de Recherche Clinique, Pôle Information Médicale Evaluation Recherche - Lyon (France), [5]University Hospital Archet, Digestive and Oncological Surgery - Nice (France), [6]Institut du Cancer de Montpellier, Surgical Oncology - Montpellier (France), [7]Institut Gustave Roussy, Surgical Oncology - Villejuif (France), [8]Centre Léon Bérard, Surgical Oncology - Lyon (France), [9]Hopital Louis Mourier, AP-HP, Digestive and Oncological Surgery - Paris (France), [10]CHU La Tronche, Digestive and Oncological Surgery - Grenoble (France), [11]University Hospital Saint Antoine, AP-HP, Digestive and Oncological Surgery - Paris (France), [12]CHU Clermond-Ferrand, Digestive and Oncological Surgery - Clermont-Ferrand (France), [13]Institut de Cancérologie de l'Ouest Paul Papin, Surigical Oncology - Clermont-Ferrand (France), [14]CHU Dijon, Digestive and Oncological Surgery - Dijon (France), [15]Hopital La Timône, AP-HM, Digestive and Oncological Surgery - Marseille (France), [16]CHU Poitiers, Digestive and Oncological Surgery - Poitiers (France), [17]CHU Reims, Digestive and Oncological Surgery - Reims (France), [18]Centre Alexis Vautrin, Surgery Dept - Nancy (France), [19]Hopital Lariboisiere AP-HP, Digestive and Oncological Surgery - Paris (France)

Objectives

Lymph node status (LNS) is a major prognostic factor in gastric cancer. Peritoneal carcinomatosis (PC) is a stage IV regardless of the LNS and associated with poor prognosis. For selected patients, cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) represent a potentially curative treatment. The clinical impact of LNS remains unclear for such patients.

The purpose of this study is to determine the clinical impact of the LNS after CRS and HIPEC for gastric PC.

Methods

Data from 172 consecutive patients who underwent complete CRS including a D2 or D.15 lymphadenectomy and HIPEC for gastric cancer with PC, in 16 French institutions from 1989 to 2014, were collected. The 7th edition of pathologic TNM stages was used to define the LNS. The Peritoneal Cancer Index (PCI) assessed extension of PC. Survival was calculated from surgery. The log-rank test was used to compare survivals and Cox models to identify the prognostic factors in univariate and multivariate analyses.

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Results

Median age was 51.4 years. 72 patients had a plastica linitis. 69.2% of tumors had a signet ring cells component. Median number of resected lymph nodes was 24 (5–67). 58.1% had spleen preservation. pN0, pN1, pN2 and pN3 represented respectively 21.5%, 13.4%, 15.1% and 50% of patients. 65.1% received a neoadjuvant chemotherapy: 86.5% in the pN0 subgroup versus 59.3% in the pN1-2-3 subgroup (p = .002). 49.8% received an adjuvant treatment: 41.9% in the pN0-1-2 versus 55.8% in the pN3 subgroup. LNS was not influenced by the extension of the PC as median PCI was similar in each group (6 in the whole population). 1-, 3- and 5-year survivals in the whole cohort were 69.3%, 27.4% and 20.2%, respectively. Median overall survival was 19.4 months. pN3 status was associated with worse survival. Median survivals in the pN0, pN1, pN2 were 23.2, 29.4, 23.9 months respectively whereas it was 13.2 months in the pN3 subgroup (p = .004). For synchronous PC (n = 138), 3- and 5-year OS for the pN0-1-2 and pN3 groups were 31.6% and 29.7% v 15.7% and 7.8%. In multivariate analysis, plastica linitis (HR: 2.565) and absence of neodajuvant therapy (HR: 2.396) were associated with a pN3 LNS. Disease-free survival was not affected by the LNS.

Conclusion

In gastric cancer with PC treated by HIPEC, the prognostic impact of LNS seems less important than in non-metastatic tumors. There is no clinical benefit of a pN0 status compared to a pN1-N2 status. Only a pN3 status is associated with worse oncological outcomes.

C39

IS CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEALCHEMOTHERAPY REASONABLE TREATMENT FOR GASTRIC SIGNET-RING CELL ADENOCARCINOMA AND LINITIS PLASTICA WITH PERITONEAL METASTASIS? CYTO-CHIP STUDY—ANCILLARY RESULTS

P.E. Bonnot[1], G. Piessen[2], F. Mercier[1], E. Decullier[3], M. Pocard[4], B. Meunier[5], J.M. Béréder[6], K. Abboud[7], F. Marchal[8], F. Quenet[9], D. Goere[10], C. Arvieux[11], S. Msika[12], D. Pezet[13], N. Pirro[14], P. Rat[15], R. Wernert[16], J. Lefevre[17], T. Courvoisier[18], P. Meeus[19], O. Glehen[1]

[1]HCL, Centre Hospitalier Lyon Sud, Dpt of Digestive and Oncological Surgery - Lyon (France), [2]University Hospital of Lille Dpt of Digestive and Oncological Surgery - Lille (France), [3]HCL, Unité de Recherche Clinique du Pole IMER - Lyon (France), [4]Hopital Lariboisiere AP-HP, Service de Chirurgie Digestie et Cancérologie - Paris (France), [5]Pontchaillou University Hospital Rennes, Dpt of Digestive and Oncological surgery - Rennes (France), [6]University Hospital Archet, Dpt of Digestive and Oncological Surgery - Nice (France), [7]CHU Saint-Etienne, Dpt of Digestive and Oncological Surgery - Saint Etienne (France), [8]Centre Alexis Vautrin, Surgery Dept - Nancy (France), [9]Institut du Cancer de Montpellie, Dpt of Oncological Surgery - Montpellier (France), [10]Institut Gustave Roussy, Dpt of Oncological Surgery - Villejuif (France), [11]CHU La Tronche, Surgery Dept - Grenoble (France), [12]Hopital Louis Mourier, AP-HP, Surgery Dept - Paris (France), [13]CHU Clermond-Ferrand, Dpt of Digestive and Oncological Surgery - Clermont Ferrand (France), [14]Hopital La Timône, AP-HM, Dpt of Digestive and Oncological Surgery - Marseille (France), [15]CHU DIJON, Dpt of Digestive and Oncological Surgery - Dijon (France), [16]Institut de Cancérologie de l'Ouest Paul Papin, Dpt of Digestive and Oncological Surgery - Angers (France), [17]Hôpital Saint Antoine, AP-HP, Dpt of Digestive and Oncological surgery - Paris (France), [18]CHU Poitiers, Dpt of Digestive and Oncological Surgery - Poitiers (France), [19]Centre Léon Bérard, Dpt of Digestive and Oncological Surgery - Lyon (France)

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Objectives

Incidence of gastric signet-ring cell adenocarcinoma (SRCa) is increasing and linitis plastica (LP) is its typical presentation. SRCa are associated with less chemosensitivity and more peritoneal metastasis (PM). Most consider PM from a gastric SRCa as an end-stage disease. Cytoreductive surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) are highly debated in those indications.

Purpose: to evaluate the impact of CRS and HIPEC in patients with PM from SRCa compared with those with PM from non-SRCa, and to assess whether the prognostic factors differed between them.

Methods

Data from 277 patients treated for gastric cancer with PM by CRS with or without HIPEC in 19 French centers from 1989 to 2014 were included. Diagnosis of an SRCa was based on the presence of isolated carcinoma cells containing mucin. Only patients treated by complete CRS with curative intent were included.

The log-rank test was used to compare survivals and Cox models to identify the prognostic factors in univariate and multivariate analyses.

Results

188 patients had an SRCa with 55.1% of LP. One tumor was a LP in the 89 patients with a non-SRCa. Patients with SRCa were more frequently female and younger, with more diffuse PM, undifferentiated and pN3 tumors. There was no difference in perioperative treatments. 124 (66%) patients in the SRCa group and 56 (62.9%) in the non-SRCa group underwent an HIPEC. Median Peritoneal Cancer Index (PCI) was higher in HIPEC sub-groups (SRCa: 7 v 2; non-SRCa: 5 v 1). PM from SRCa was associated with worse survival. After CRS, with or without HIPEC, 3-year OS was 14% in the SRCa v 38.4% in the non-SRCa (P = <.001). In the SRCa group, HIPEC was associated with better survival on multivariate analysis than CRS alone (median OS: 16.3 v 11 months, HR, 0.526; 95% CI, 0.34–0.81; P = .003). LP, tumor grade, PCI and adjuvant treatment were independent prognostic factors for OS. In the non-SRCa group, effect of HIPEC was more significant with 3- and 5-year OS of 50.1% and 45.4 v 17% and 17% (P = .004). ASA score, PCI and nodal status were independent prognostic factors for OS.

Conclusion

PM from gastric SRCa or non-SRCa have distinct presentations and presence of SRC significantly impairs prognosis. However, HIPEC appears as a valuable option therapy on selected patients versus CRS alone for resectable PM from SRCa. Concerning PM from non-SRCa, this study is currently the best evidence that HIPEC can offer similar survival rates to non-metastatic tumors.

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C40
PERITONEAL CARCINOMATOSIS OF MIXED ADENOENDOCRINE CARCINOMA TREATED BY CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC): AN INTERNATIONAL REGISTRY

F. Mercier[1], P. Cashin[2], W. Ceelen[3], P.E. Bonnot[1], L. Villeneuve[1], G. Passot[1], E. Levine[4], O. Glehen[1]

[1]Hospices Civils de Lyon- Lyon Sud Hospital - Pierre Benite (France), [2]Uppsala University - Uppsala (Sweden), [3]Ghent University Hospital - Ghent (Belgium), [4]Wake Forest University Baptist Medical Center - Winston Salem (United States)

Objectives

Peritoneal carcinomatosis from mixed adenoendocrine carcinoma (MANEC) or Goblet cell carcinoma is a rare type of carcinomatosis and an aggressive form of appendiceal tumor. Primary metastatic sites is the ovary followed by peritoneal dissemination. Resistance to chemotherapy of these tumors (such as 5-FU and FOLFOX) contribute to their poor prognosis. Few reports suggest that cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) can prolong survival in those aggressive cancer. Our aim was to improve our understanding of the disease and to document the survival of patients treated by CRS and HIPEC through an international registry of expert centers.

Methods

A prospective multicenter international database was retrospectively searched to identify all patients with MANEC tumor and peritoneal metastases who underwent CRS and HIPEC through the Peritoneal Surface Oncology Group International (PSOGI). The post-operative complications, long-term results, and principal prognostic factors were analyzed.

Results

The analysis included 83 patients. The median follow-up was 47 months. The a median overall survival (OS) of 27,4 months, the 3- and 5-year OS was 39.8% and 27.2%. The 5-year OS was 35.3% for patients in which complete CRS was achieved vs. 0% for the incomplete CRS group (HR 3,03 IC95 1.79–6.16; p = 0.014). Lymph node involvement and postoperative chemotherapy were also predictive of a worse prognosis. There were 3 postoperative deaths, and 30% of the patients had major complications.

Conclusion

CRS and HIPEC may increase long-term survival in selected patients with peritoneal metastases of MANEC origin, especially when complete CRS is achieved. When realizing these procedures for MANEC, morbidity and mortality are similar to other origin of carcinomatosis. CRS and HIPEC should be undertaken with caution when complete CRS cannot be achieved. Randomized control trials are needed to confirm CRS and HIPEC as the gold standard in this pathology.

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C41
PROGNOSTIC IMPORTANCE OF GENETIC ALTERATIONS IN COLORECTAL PERITONEAL METASTASES

H. Birgisson[1], M. Enblad[1], W. Graf[1], A. Terman[2], P. Pucholt[3], B. Viklund[3], A. Isaksson[3]

[1]Uppsala University, Department of Surgical Sciences - Uppsala (Sweden), [2]Uppsala University, Department of Immunology, Genetics and Pathology - Uppsala (Sweden), [3]Uppsala University, Department of Medical Sciences; Science for Life Laboratory - Uppsala (Sweden)

Objectives

Genetic alterations in colorectal peritoneal metastases (PM) are largely unknown. The aim of this study was to describe genetic alterations in colorectal PM and identify alterations associated with prognosis after cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC).

Methods

All patients with non-pseudomyxoma peritonei PM, originating from an invasive appendiceal or colorectal adenocarcinoma, treated with CRS and HIPEC in Uppsala Sweden, between 2004 and 2015, were included (n = 114). DNA derived from formalin-fixed paraffin-embedded (FFPE) specimens were analysed for whole-genome copy number alterations (CNA) using molecular inversion probe arrays.

Results

Successful copy number (CN) analysis was performed in 52 patients (26 right colon, 21 left colon, 5 rectal). There was no difference in survival between patients with successful and unsuccessful CN analysis. There was a wide distribution of genomic composition, ranging from minimal CNA to total aneuploidy. In particular, gain on parts of chromosome 1p and major parts of 15q were associated with poor survival. A combination of gain on 1p and 15q was associated with poor survival, also after adjustment for differences in peritoneal cancer index and completeness of cytoreduction score (HR 5.96 95%CI 2.19–16.18). These patients had a mean CN of 3.19 compared to 2.24 in patients without gains.

Conclusion

This study shows that there are extensive but varying degrees of CNA in colorectal PM. Gain on parts of chromosome 1p and on major parts of chromosome 15q were significantly associated with poor survival after CRS and HIPEC.

C42
COMPARISON BETWEEN PCI AND DUTCH REGION COUNT AS A PROGNOSTIC TOOL IN PATIENTS WITH COLORECTAL PERITONEAL METASTASES

W. Van Eden, F. Verheij, N. Kok, A. Aalbers

Netherlands Cancer Institute - Amsterdam (Netherlands)

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Objectives

Cytoreductive surgery (CRS) followed by hyperthermic intraperitoneal chemotherapy (HIPEC) is the preferred treatment in selected patients with colorectal peritoneal metastases (PM) and significantly improves survival. Preoperative assessment of the peritoneal tumour load identifies eligible patients for CRS-HIPEC. The Peritoneal Cancer Index (PCI) is a validated, internationally used tool to address extent of peritoneal metastases. This score is rather complex for professionals not performing CRS-HIPEC. The Dutch region count is a simplified classification which has been shown to correlate well with survival. This study aimed to compare the PCI and Dutch region count as a prognostic tool for CRS-HIPEC.

Methods

In this retrospective cohort study patients with colorectal PM who were intentionally treated with CRS-HIPEC in 2016 and 2017 were included. PCI and Dutch region count were recorded during exploratory laparotomy before CRS-HIPEC started. The correlation coefficient between the scoring tools was calculated. Diagnostic values were calculated for different cut-off values of the PCI based on international literature in combination with the Dutch region count, where the PCI was the gold standard. Survival analyses were performed.

Results

Seventy-six patients were included in this study of whom 67 underwent CRS-HIPEC. A Spearman correlation coefficient of 0.883 was found for the continuous scores of the region count and the PCI. A PCI-cut-off value of 20 was associated with a sensitivity of 90.6% and a specificity of 83.3% for a cut-off value of 5 for the region count. The Spearman correlation coefficient for the region count during DLS and the region count during CRS-HIPEC was 0.901.

Conclusion

The region count and the PCI are both useful tools to identify patients that are eligible for CRS-HIPEC and they correlate pretty well. The region count however may be preferable during preoperative imaging and during diagnostic laparoscopy (DLS), or in centres with less experience because of its simplicity.

C43

THE VOLUME TIME INDEX (VTI): THE RATIO OF PERITONEAL CANCER INDEX TO TIME FROM PRIMARY TUMOUR RESECTION IS A PROGNOSTIC SURROGATE OF TUMOUR AGGRESSIVENESS AND BIOLOGY IN PATIENTS WITH COLORECTAL CANCER WITH PERITONEAL METASTASES UNDERGOING CYTOREDUCTIVE SURGERY AND INTRAPERITONEAL CHEMOTHERAPY

M.A. Kozman, O.M. Fisher, S.J. Valle, N. Alzahrani, W. Liauw, D.L. Morris

St George Hospital - Liver and Peritonectomy Unit - Sydney (Australia)

Objectives

Peritoneal cancer index (PCI) is an important prognostic factor in patients with colorectal cancer with peritoneal metastases (CRPM) undergoing cytoreductive surgery (CRS) and intraperitoneal chemotherapy (IPC). However, analysis of PCI in isolation fails to consider the time period over which the extent of peritoneal disease develops. The volume-time index (VTI) is the ratio between PCI and time from resection of primary colorectal cancer and may function as a surrogate of underlying tumour biology. Its relevance to patient survival has not yet been reported.

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Methods

A retrospective cohort study of 182 patients with CRPM managed from 1996 to 2017 with CRS/ IPC was performed by analysing the impact of the VTI on patient outcomes.

Results

As stratified by high vs low VTI groups, median overall survival (OS) was 23 months (95% 17–46) vs 44 months (95% 35–72) with a difference in 5-year OS of 20.3% (95%CI 10.2–40.4) vs 40.1% (95%CI 29.7–54.1), p = 0.002. Median recurrence free survival (RFS) was 11 months (95% 10–17) vs 11 months (95% 8–13) with no statistically significant difference in 5-year RFS. On multivariable analysis, an elevated VTI was independently associated with poorer OS (adjusted HR 2.88, 95%CI 1.39–5.93, p = 0.004).

Conclusion

VTI is an independent prognostic factor for OS in patients with CRPM undergoing CRS/ IPC. This simple index behaves as a surrogate of tumour aggressiveness and biology and provides a useful adjunct for decisions regarding treatment allocation.

C44

CEA TO PERITONEAL CARCINOMATOSIS INDEX (PCI) RATIO IS PROGNOSTIC IN PATIENTS WITH COLORECTAL CANCER PERITONEAL CARCINOMATOSIS UNDERGOING CYTOREDUCTION SURGERY AND INTRAPERITONEAL CHEMOTHERAPY

M.A. Kozman, O.M. Fisher, B.J. Rebolledo, R. Parikh, S.J. Valle, N.A. Alzahrani, W.L. Liauw, D.L. Morris

St George Hospital - Liver and Peritonectomy Unit (Australia)

Objectives

Serum tumour markers are prognostic in patients with colorectal cancer peritoneal carcinomatosis (CRPC) undergoing cytoreductive surgery (CRS) and intraperitoneal chemotherapy (IPC). Assessment of the ratio of tumour marker to volume, as depicted by peritoneal carcinomatosis index (PCI), and how this may affect overall (OS) and recurrence free survival (RFS) has not been reported.

Methods

A retrospective cohort study of all patients with CRPC managed from 1996–2016 with CRS and IPC was performed by analysing the survival effect of the ratio of preoperative serum CEA, CA19.9 and CA125 to PCI.

Results

Of 260 patients included, those with low CEA/PCI ratio (<2.3) had longer median OS (56 vs 24 months, p = 0.001) and RFS (13 vs 9 months, p = 0.02). The prognostic impact of CEA/PCI ratio was most pronounced in patients with PCI ≤ 10 (OS of 72 vs 30 months, p < 0.001; RFS of 21 vs. 10 months, p = 0.002). In multivariable analysis, elevated CEA/PCI ratio was independently associated with poorer OS (adjusted HR 1.85, 95%CI 1.11–3.10, p = 0.02) and RFS (adjusted HR 1.58, 95%CI 1.04–2.41, p = 0.03).

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Conclusion

CEA/PCI ratio is an independent prognostic factor for OS and RFS in CRPC. This novel approach allows both tumour activity and volume to be accounted for in one index, thus potentially providing a more accurate indication of tumour biological behaviour.

C45
CYTOREDUCTIVE SURGERY COMBINED WITH HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR COLORECTAL OR APPENDICEAL PERITONEAL METASTASIS

Y. Gohda, K. Deguchi, Y. Nagai, A. Kataoka, K. Ohtani, T. Kiyomatsu, N. Kokudo, H. Yano

National Center for Global Health and Medicine - Tokyo (Japan)

Objectives

The current study retrospectively reviewed the outcomes of the multimodal treatment for peritoneal metastasis from colorectal or appendiceal cancer (PM-CRC/AC).

Methods

Thirty-eight patients with PM-CRC/AC underwent neoadjuvant intravenous±intraperitoneal chemotherapy followed by CRS+HIPEC between 2010 and 2016. Patients with pseudomyxoma peritoneal or those who had metastasis in other distant organs were excluded. Intravenous chemotherapy was according to colorectal cancer on days 1 and 15, Paclitaxel was administered intraperitoneal at 20 mg/m^2 on days 1, 8 and 15. NIPS was repeated every 4 weeks for a period from three to six months.

Results

The median age was 54 (range, 22–76). Primary tumours were in appendix in 11 patients and in colorectum in 27. Seventeen were synchronous and 21 were metachronous. All patients had neoadjuvant intravenous±intraperitoneal chemotherapy. Neoadjuvant intravenous and intraperitoneal chemotherapy (NIPS) was given in 22 patients (63%). The median Peritoneal Cancer Index score was 9 (range, 2–33). NIPS was successfully completed in 22 patients (92%). Dose reduction of intravenous chemotherapy was required in 42%, Grade III adverse events were observed in 38% of the patients, most of which were cytopenia. The median pre-treatment PCI was 14 and post-treatment PCI was 10. The response rate was 42% with 8 SDs and 6 PDs.

CC-0 was achieved in 71% of the patients. The median hospital stay was 22 days (range, 9–281). Clavien-Dindo Grade III morbidity was found in 6 patients with no mortality. During the median follow-up period of 25 months (range, 7–96), 26 patients (68%) developed recurrence with most (21 patients) occurring in the peritoneum. The 3-year overall survival and disease-free survival rates were 62% and 26%. The 3-year disease-free survival of the patients for whom CC-0 was achieved was 34%.

Conclusion

A multimodal treatment encompassing CRS+HIPEC and neoadjuvant chemotherapy might further improve the outcomes for colorectal or appendiceal peritoneal metastasis. Patient selection is likely to be crucial.

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C46
THE SHORT-TERM ONCOLOGIC OUTCOMES OF HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) AFTER CYTOREDUCTIVE SURGERY TO TREAT PERITONEAL CARCINOMATOSIS FROM COLORECTAL CANCER: A PROSPECTIVE STUDY OF A TERTIARY REFERRAL CENTER IN SOUTH KOREA

E.J. Park, Y. Jeon, J. Kang, S.H. Baik

Division of Colon and Rectal Surgery, Department of Surgery, Yonsei University College of Medicine - Seoul (Korea, Republic of)

Objectives

This aim of this study was to evaluate both clinical and oncologic outcomes of cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with peritoneal carcinomatosis from colorectal cancer in South Korea.

Methods

From July 2014 to October 2017, we evaluated a total of 94 consecutive patients who underwent cytoreductive surgery with hyperthermic intraperitoneal chemotherapy to treat colorectal cancer with peritoneal carcinomatosis in the Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea. The patients who diagnosed appendiceal cancer or pseudomyxoma peritoneal were excluded in this study. The perioperative outcomes and short-term oncologic outcomes were evaluated. The 1-year and 2-year survival rates were calculated by the Kaplan-Meier method and the log-rank test.

Results

There were 44 males and 50 females with the mean age of 54.8 years old. The mean peritoneal cancer index (PCI) was 10.9 ± 9.6. There were PCI ≤ 9 of 51.1%, PCI 10–19 of 26.6%, and PCI ≥ 20 of 22.3%. The completeness of cytoreduction score (CC-score) was CC-0 of 86.2%, and CC-1 of 13.8%. The mean operation time was 9.3 ± 3.6 hours. The mean hospital stay was 21.6 ± 15.7 days (range, 8–98 days). There were 11 patients (11.7%) with postoperative 30 day re-admission. The median overall survival was 31.0 month (95% CI 21.4–40.6) and progression free survival was 12.0 month (95% CI 9.0–15.0). According to PCI score, the 1-year overall survival was 84.2% of PCI ≤ 9 group, 75.7% of PCI 10–19 group, 56.6% of PCI ≥ 20 group, and the 2-year overall survival was 66.3% of PCI ≤ 9 group, 50.5% of PCI 10–19 group, and 15.1% of PCI ≥ 20 group (p = 0.020). In addition, according to the outcomes of cytoreduction completeness, the 1-year overall survival was 83.5% in the patients with CC-0 and 60.4% with CC-1. The 2-year overall survival was 55.5% with CC-0 and 20.1% with CC-1 (p = 0.085). The 1-year progression-free survival was 54.6% of PCI ≤ 9, 32.9% of PCI 10–19, 58.1% of PCI ≥ 20 (p = 0.218). The 1-year progression-free survival was 56.5% of CC-0 and 38.7% of CC-1 patients (p = 0.091).

Conclusion

The clinical and oncologic outcomes of cytoreductive surgery with HIPEC to treat colorectal cancer with peritoneal carcinomatosis were acceptable compared with previous reports. Both low PCI and the completeness of cytoreduction were regarded as important factors to affect oncologic outcomes.

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C47
INVOLVEMENT OF THE RIGHT UPPER QUADRANT IS PREDICTIVE OF AN INFERIOR SURVIVAL IN PATIENTS WITH COLORECTAL PM UNDERGOING COMPLETE CYTOREDUCTIVE SURGERY AND HIPEC – A RETROSPECTIVE STUDY FROM THE INDIAN HIPEC REGISTRY

A. Bhatt[1], S. Mehta[2], S. Zaveri[3], M. Ray[4], P. Kammer[5], D. Damodaran[6], S. Sinukumar[7], R. Seshadri[8]

[1]Zydus hospital - Ahmedabad (India), [2]Saifee Hospital - Mumbai (India), [3]Manipal Hospital - Bangalore (India), [4]All India Institute of Medical Sciences - New Delhi (India), [5]Global Hospital - Hyderabad (India), [6]MVR Cancer Center and Research Institute - Calicut (India), [7]Jehangir Hospital - Pune (India), [8]Cancer Institute (WIA) - Chennai (India)

Objectives

In patients with colorectal peritoneal metastases undergoing complete cytoreductive surgery (CC-0/1) and HIPEC and having involvement of the right upper quadrant (RUQ) our goals were:

To study the pattern of peritoneal dissemination To study the impact of RUQ involvement on perioperative outcomes, disease free survival (DFS) and overall survival (OS).

Methods

A retrospective analysis of patients treated between Jan 2013 to Dec 2017 was performed. RUQ was defined as region 1 in Sugarbaker's peritoneal cancer index (PCI). A comparison of PCI and the small bowel PCI (sum of the PCI in regions 9–12) in patients with and without RUQ involvement was made. The impact of RUQ involvement of DFS and OS was analyzed.

Results

Of the 67 patients undergoing complete CRS (CC-0/1) and HIPEC (n = 62) included in the study, the RUQ was involved in 31 patients and uninvolved in 36 patients. Patients with RUQ involvement had a higher median PCI (18 versus 6), a higher small bowel PCI ($p < 0.001$) and a higher proportion of mucinous tumors ($p < 0.01$). The proportion of CC-1 versus CC-0 resections ($p = 0.03$) was higher in these patients and and a larger proportion received neoadjuvant chemotherapy (NACT) ($p < 0.001$). All patients without RUQ involvement had a PCI of less than 12 compared to 22.5% with RUQ involvement. In case of left upper quadrant involvement (region 3), RUQ involvement was present in all except two patients. The 90-day grade 3–4 morbidity ($p = 0.08$) and 90-day mortality ($p = 0.52$) was similar between the two groups. 77.4% with and 94.4% without RUQ involvement completed 6 months of perioperative chemotherapy ($p = 0.04$). Involvement of the RUQ was an independent predictor of an inferior DFS [Hazard ratio 2.097 (95% CI- 1.067–4.122); $p = 0.03$]. The median OS was inferior ($p = 0.02$) in these patients though it did not reach statistical significance on multivariate analysis. The only independent predictor of an inferior OS was 90-day grade 3–4 morbidity (<0.001).

Conclusion

Involvement of the RUQ is seldom an isolated event in colorectal PM and usually presents with extensive disease. There is an inferior DFS and OS following complete CRS and HIPEC in this group that is not offset by the use of NACT. Involvement of this region can be determined on pre-op imaging or staging laparoscopy and could be incorporated into patient selection tools and normograms as a poor prognostic factor and a predictor of advanced disease. New treatment strategies need to be devised to improve outcomes in this group of patients.

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C48
HIPEC WITH GEMCITABINE AS AN ADJUVANT LOCOREGIONAL TREATMENT AFTER RADICAL SURGERY IN PANCREATIC CANCER. PRESENTATION OF THE CLINICAL TRIAL N-2016-004298-41

E.P. García Santos, D. Padilla Valverde, P. Villarejo Campos, S. Sánchez García, J. Martín Fernández

Hospital General Universitario de Ciudad Real - Ciudad Real (Spain)

Objectives

A population of stem cells with malignant transformation called pancreatic tumor stem cells with high locoregional invasion capacity has been identified as the origin of pancreatic cancer. We present the project of a clinical trial in which we administered HIPEC with Gemcitabine to improve the survival rates of the patients by decreasing the recurrence of the disease.

Methods

* Phase II-III clinical trial. Experimental, controlled, randomized, parallel clinical study 1: 1.

* Main variables: 1- Global survival 2. Recurrence 3. Disease-free period * Secondary variables: 1-Adverse effects, complications, and mortality during patient admission. 2-Other variables included in this study are: age, tumor stage, duration of the procedure, and hospital stay.

* Population: 42 patients with a diagnosis of adenocarcinoma of the pancreas, who will undergo surgery with curative intent. *Group I. Cytoreductive surgery and adjuvant treatment (4 cycles of Gemcitabine iv). *Group II. Cytoreductive surgery together with HIPEC with Gemcitabine, 120 mg/m^2 for 30 minutes and adjuvant treatment.

For the realization of HIPEC we use the model developed for closed access and CO2 recirculation (PRS Combat®, Galmaz Biotech SL).

Results

There were no technical or hemodynamic complications during the procedure. There were also no clinical or analytical complications associated with the possible toxicity of the drug.

Conclusion

The use of HIPEC can achieve a decrease in the tumor progression of pancreatic cancer by reducing the neoplastic volume and subpopulation of pancreatic tumor stem cells, improving the survival of the patient, and decreasing the recurrence of the disease. This study is open to centers that want to collaborate in the effort to discover an effective therapy that will improve survival rates.

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C49
MORBIMORTALITY OF PATIENTS UNDERGOING CITOREDUCTION+CLOSED HIPEC WITH CO2 AGITATION SYSTEM: A MULTICENTRE STUDY

A. Gutierrez[1], R. Gomez[2], A. Lopez[2], S. Sanchez[3], P. Villarejo[3], D. Padilla[3], I. Manzanedo[4], F. Pereira[5], E. Perez-Viejo[4], L. Gonzalez[6], E. Lopez-Tomassetti[6], J.R. Hernandez[6], E. Diaz[7], I. Fabra[7], A. Titos[8], M. Pitarch[9], F. Ochando[10], F.J. La Cueva[11]

[1]Jefe Clínico Cirugía Hospital Universitario Príncipe de Asturias (GECOP) - Alcala De Henares. Madrid (Spain), [2]FEA Cirugía Hospital Universitario Príncipe de Asturias (GECOP) - Alcala De Henares. Madrid (Spain), [3]FEA Cirugía Hospital Universitario Ciudad Real (GECOP) - Ciudad Real (Spain), [4]FEA Cirugía Hospital Universitario Fuenlabrada (GECOP) - Madrid (Spain), [5]Jefe Cirugía Hospital Universitario Fuenlabrada (GECOP) - Madrid (Spain), [6]FEA Cirugía Hospital Insular de Gran Canaria - Gran Canaria (Spain), [7]FEA Cirugía Hospital Universitario Madrid San Chinarro - Madrid (Spain), [8]FEA Cirugía Hospital Universitario de Malaga - Malaga (Spain), [9]MIR Cirugía Hospital Universitario de Malaga - Malaga (Spain), [10]FEA Cirugía Hospital Universitario Fundacion Alcorcon - Madrid (Spain), [11]Jefe Clinico Cirugía Hospital Universitario de Elche - Elche (Spain)

Objectives

There are two ways of carrying out Hyperthermic IntraPEritoneal Chemotherapy: the open (or “Coliseum") technique and the closed technique. There is no study that demonstrates a greater long-term clinical benefit of either technique. In order to combine the potential benefits of both techniques, a closed technique HIPEC with CO2-Agitation (PRS+A) was launched in 2011. The objective of this study is to analyse the morbidity and mortality results of this technique.

Methods

A multicenter, retrospective study based on a common prospective database of 318 patients, chosen without specific selection criteria and treated with the Closed HIPEC with CO2-Agitation (PRS+A) technique. Interoperative and postoperative complications were classified according to the Clavien-Dindo 2004 scale. A descriptive statistical analysis was performed for qualitative and quantitative variables.

Results

Of the 318 patients included in the study, 65.7% were women. The average age was 58 years. The origin of carcinomatosis was colon in 151 cases, ovarian in 101, gastric in 39, pseudomyxoma in 16, mesothelioma in 6 and others in 5 cases. 4 or more surgical procedures were performed in 136 patients. A total of 102 patients (32%) presented some type of complication, with type III / IV in 38 patients (11%). During the HIPEC procedure, complications occurred in 7 patients (2.2%): Other complications included 5 hyperglycemias (higher than 400), one case of severe metabolic acidosis and one case of a severe allergic reaction to oxaliplatin. These complications did not cause an increase in ICU stay. No statistical increase in risk was found during the HIPEC procedure related to the drug used, the age of the patient, the PCI or the number of surgical procedures performed. Operative mortality was 2% (7 patients), none of which were directly related to the HIPEC procedure.

Conclusion

Cytoreduction with the closed HIPEC technique with CO2 agitation (PRS-A) is a safe technique, with acceptable morbidity and mortality rates, similar to other surgical procedures of high complexity.

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C50
BIOMARKER CONCORDANCE BETWEEN PRIMARY COLORECTAL CANCER AND PERITONEAL METASTASES

D. Bhullar[1], S. O'dwyer[2], O. Aziz[2]

[1]University of Manchester Medical Student, Division of Medical Education. - Manchester (United Kingdom), [2]Colorectal and Peritoneal Oncology Centre, the Christie NHS Foundation Trust - Manchester (United Kingdom)

Objectives

The use of biomarkers in predicting outcome from anti-EGFR based treatments in metastatic colorectal cancer is well established, with emphasis now on research into the prognostic impact of multiple biomarker status. Concordance between the primary tumour and metastatic site in these biomarkers is an important factor that should be taken into account when determining the impact of any treatment, especially in patients with colorectal cancer peritoneal metastases (CRPM). This study aims to systematically review the literature with regards to concordance between the primary colorectal cancer and its metastatic site including CRPM.

Methods

A systematic review of all studies reporting on concordance between primary colorectal cancers and their metastatic sites published between 1991 and 2017 was conducted according to the PRISMA criteria using PubMed, MEDLINE, OVID, EMBASE, and Google Scholar databases. Two independent reviewers independently extracted the data.

Results

57 studies reporting on biomarker concordance in 3178 patients were included. Median biomarker concordance included: KRAS = 93.8% (51 Studies), NRAS = 100% (11 Studies), BRAF = 99.4% (22 Studies), PIK3CA = 93.6% (17 Studies), PTEN = 92% (10 Studies), TP53 = 92.9% (12 Studies), APC = 89.5% (10 Studies), SMAD4 = 94.3% (6 Studies), EGFR = 67% (5 Studies), and MSI/MMR = 94.5% (5 Studies). Results for median concordance according to metastatic site were liver (43 studies) = 99% (39.4–100%), lung (29 studies) = 100% (44.4–100%), and lymph nodes (24 studies) = 96% (67.9–100%). 16 studies reported on CRPM but included these with other metastatic sites in their analysis. One study reported a concordance for CRPM of 100%. Median absolute concordance in multiple biomarkers was 81% (5–95%).

Conclusion

Whilst there is a relatively concordant biomarker relationship between primary colorectal cancers and their corresponding liver and lung metastases in key biomarkers, there remains a lack of data for CRPM patients. Establishing biomarker concordance in this group may help to identify why patients with CRPM have a poorer prognosis and help to personalise hyperthermic intraperitoneal chemotherapy in this patient group.

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C51
EXOSOMAL MICRORNA PROFILES IN PERITONEAL FLUIDS AS A THERAPEUTIC BIOMARKER FOR PERITONEAL METASTASIS OF GASTRIC CANCER

H. Ohzawa[1], Y. Kumagai[2], H. Yamaguchi[3], Y. Hosoya[2], N. Sata[2], J. Kitayama[2]

[1]Center for Clinical Research, Jichi Medical University Hospital - Tochigi (Japan), [2]Department of Gastrointestinal Surgery, Jichi Medical University - Tochigi (Japan), [3]Department of Clinical Oncology, Jichi Medical University Hospital - Tochigi (Japan)

Objectives

Peritoneal metastasis (PM) frequently occurs in patients with gastric cancer and has poor prognosis even with systemic chemotherapy. Intraperitoneal chemotherapy (IPC) using paclitaxel (PTX) combined with systemic chemotherapy has demonstrated a remarkable clinical efficacy for gastric cancer with PM. However, there is no reliable biomarker to reflect the response of peritoneal lesions as well as to predict the outcome of the patients receiving IPC. Although peritoneal fluids are considered to contain many factors derived from disseminated tumor cells in peritoneal cavity, little information is available so far. In this study, we examined exosomal miRNA profiles derived from peritoneal fluids in patients with gastric cancer and explored possible biomarkers useful for IPC of the patients with PM.

Methods

Peritoneal fluids were collected from 2 groups; with or without PM. Peritoneal fluids were obtained either laparoscopically, during open surgery or from subcutaneous infusion port connected to an intraperitoneal catheter. Exosomal fractions were isolated using ultracentrifuge method (150,000 xg, 70 min, 4°C) and the presence of exosome was confirmed with nanotracking analysis. Total RNA including small RNA was extracted from exosomal fractions and expression analyses of miRNAs were performed using RT-PCR.

Results

At first, we comprehensively analyzed the expression of miRNAs between 11 samples with PM and 14 samples without PM and identified 11 miRNAs which showed particularly different expression pattern between the 2 groups. Among them, 4 miRNAs (miR-21-5p, miR-223-3p, miR-342-3p and miR-92a-3p) were selected and further analyzed using 51 samples derived from the peritoneal fluids of gastric cancer. Expression of these 4 miRNAs were significantly up-regulated in samples with PM which was consistent with former analysis. Moreover, expression of miR-21-5p was significantly upregulated in in samples fromT4 tumor (invaded serosa or adjacent structure) as compared with those from T1 to T3 tumor.

Conclusion

We identified several dysregulated exosomal miRNAs derived from peritoneal fluids of the patients with PM from gastric cancer, which were supposed to reflect the tumor burden on peritoneum. Exosomal miRNA profiles might be useful biomarkers to determine the presence of PM as well as the response to IPC.

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C52
GENERATION AND VALIDATION OF AN IMMUNOHISTOCHEMICAL PANEL TO PREDICT CHEMOSENSITIVITY AND PROGNOSIS IN PATIENTS WITH COLORECTAL PERITONEAL CARCINOMATOSIS

J.W.S. Tan, N.B. Shannon, H.L. Tan, X. Qiu, J. Hendrikson, W.H. Ng, C.S. Chia, G.H.C. Tan, K.C. Soo, O.L. Kon, C.A.J. Ong, M.C.C. Teo

National Cancer Centre Singapore - Singapore (Singapore)

Objectives

To increase our ability to stratify patients who will benefit from CRS/HIPEC with Mitomycin C, allow tailoring of the choice and dosage of drug used in HIPEC, and in the process, improve clinical management of these patients.

Methods

A gene signature of sensitivity to Mitomycin C was determined using data from The Cancer Genome Atlas (TCGA). Validation was performed with immunohistochemical staining on clinical formalin-fixed paraffin embedded (FFPE) samples from a patient cohort with colorectal peritoneal carcinomatosis (CPC) who underwent CRS/HIPEC in our institution (n = 62). Using overall survival as a surrogate marker, prognostic significance of chemosensitivity gene signature was determined using a logistic regression model.

Results

Using the gene expression data and clinical information from TCGA, we identified three potential predictors of sensitivity to Mitomycin C in patients with CPC and successfully optimized them for automated immunohistochemical staining (PAXIP1, SSBP2, DTYMK). Patients exhibiting lower expression of PAXIP1 had significantly poorer survival as compared to those with higher protein expression ($p = 0.038$). There was a trend towards poorer survival in patients with lower expression of SSBP2 ($p = 0.134$) and no difference was observed for DTYMK ($p = 0.715$). Utilizing PAXIP1 and SSBP2 as a combined IHC panel, significantly poorer survival was observed in patients with two dysregulated genes as compared to one or no dysregulated gene ($p = 0.012$). This 2-gene signature independently predicted survival in a multivariable Cox regression model with other known clinicopathological variables including peritoneal carcinomatosis index (PCI) and TNM staging system (hazard ratio, 4.050; 95% CI, 1.242–13.207; $p = 0.020$).

Conclusion

We identified and validated a prognostic signature for Mitomycin C sensitivity that independently predicts for survival. This panel provides us the potential to better stratify patients who will benefit from CRS/HIPEC with Mitomycin C and enables tailoring of the choice and dosage of drug used in HIPEC.

C53
A MOUSE MODEL OF COLORECTAL PERITONEAL CARCINOMATOSIS DRIVEN BY PARACRINE SIGNALLING PROVIDES A UNIQUE OPPORTUNITY FOR DRUG TESTING

W.H. Ng, J. Hendrikson, X. Qiu, J.W.S. Tan, N.B. Shannon, C.S. Chia, G.H.C. Tan, K.C. Soo, O.L. Kon, C.A.J. Ong, M.C.C. Teo

National Cancer Centre Singapore - Singapore (Singapore)

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Objectives

To develop a mouse model of colorectal peritoneal carcinomatosis (CPC) by utilizing patient derived cell-free ascites to stimulate paracrine signalling necessary for tumour formation.

Methods

2 cell lines representative of PC were identified and optimization experiments performed to determine the number of cells needed to form intra-peritoneal colonies 3 weeks after injection. Ascites derived from patients with PC were collected and centrifuged at 2000 rpm to remove cellular debris. A biochemical screen was performed to identify cell-free ascites which stimulated proliferation of cell lines along with downstream activation of signalling pathways necessary for metastasis *in vitro*. Cells were injected intra-peritoneally into immunocompromised Balb/c nude mice of 6 to 8 weeks of age. 100 µl of cell-free ascites of different concentrations (5% and 50%) were injected intraperitoneally every 3 days up to 21 days. Tumour burden was quantified with a modified Peritoneal Carcinomatosis Index (PCI).

Results

The number of cells necessary to form intraperitoneal tumours was cell-line dependent (Range: 10 to 25 million). Intraperitoneal inoculation of high dose cell-free ascites (50%) led to a significant increase in tumour burden compared to low dose ascites (5%) and control (normal saline). The modified PCI score were 21, 10 and 10 in the high dose ascites, low dose ascites and control groups respectively ($p = 0.0094$). Histological examination and validation with immunohistochemistry of peritoneal nodules confirmed the presence of malignant cells in the peritoneal nodules.

Conclusion

We have generated a reliable and efficient *in vivo* mouse model of PC that is dependent on paracrine signalling, activated by cell-free ascites collected from patients with PC. This provides a platform to test novel inhibitors and chemotherapeutic agents in the treatment of PC.

C54

CLINICOPATHOLOGICAL DIFFERENCES AMONG COLORECTAL CANCER PATIENTS WITH DIFFERENT SITES OF METASTASIS

N. Chandran[1], G. Tan[2], M. Teo[2], C. Chia[2]

[1]Duke-NUS Medical School - Singapore (Singapore), [2]National Cancer Centre Singapore - Singapore (Singapore)

Objectives

20% of patients with colorectal cancer (CRC) are diagnosed with stage IV disease at presentation. The most common site of metastasis is liver, followed by peritoneum and lung. Currently, there are limited studies that look at differences in clinicopathological factors among CRC patients with different sites of metastasis.

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Methods

Patients with Stage IV CRC with a single site of metastasis who were treated with palliative chemotherapy between January 2013 to December 2015 at the National Cancer Centre Singapore were analysed. Comparisons were made between patients with liver, lung and peritoneal metastasis.

Results

Out of 169 patients with metastatic CRC, 89 (53%) patients had liver metastasis, 63 (37%) patients had peritoneal metastasis and the remaining 17 (10%) patients had lung metastasis. Four parameters were significantly different between patients with these sites of metastasis including: patients who were hospitalized (P = 0.022), patients with intestinal obstruction (P = 0.047), patients with left sided tumour (P = 0.038) and those who have distant metastasis at the time of diagnosis (P = 0.003).

Conclusion

Patients with different sites of metastasis have different clinicopathological factors which may inform us about the metastatic spread pattern of patients with CRC.

C55

POSTOPERATIVE ABDOMINAL INFECTIONS AFTER RESECTION OF T4 COLON CANCER INCREASE THE RISK OF INTRA-ABDOMINAL RECURRENCE

C. Klaver[1], K. Wasmann[1], M. Verstegen[2], J. De Wilt[2], I. Nagtegaal[2], J. Van Der Bilt[3], P. Tanis[1], B. Van Ramshorst[4], H. Van Santvoort[4], A. Wolthuis[5], A. D'hoore[5]

[1]AMC - Amsterdam (Netherlands), [2]Radboudumc - Nijmegen (Netherlands), [3]Flevoziekenhuis - Almere (Netherlands), [4]Antonius Ziekenhuis - Nieuwegein (Netherlands), [5]UZ Leuven - Leuven (Belgium)

Objectives

Patients with pT4 colon cancer are at risk of developing intra-abdominal recurrence. Infectious complications have been shown to negatively influence DFS and OS in stage I-III colon cancer. The aim of this study was to determine whether surgical site infections (SSIs) also increase the risk of intra-abdominal recurrence in pT4 colon cancer patients.

Methods

All consecutive patients with a pT4N0-2M0 colon cancer from four centres between January 2000 and December 2014 were included. Patients were categorized into those with and without a postoperative (<30 days) SSI, including both deep incisional as well as organ/space SSIs. The primary outcome was intra-abdominal recurrence (including local/incisional recurrence, peritoneal metastases) assessed using Kaplan-Meier and Cox regression analyses. Secondary outcome measures were disease free survival (DFS) and overall survival (OS).

Results

Of all 420 patients, 62 (15%) developed a SSI. The 5-year intra-abdominal recurrence rate was 44% and 27% for patients with and without a SSI, respectively (p = 0.011). In multivariate analysis, SSIs were significantly associated with the risk of intra-abdominal recurrence (HR 1.807 (1.091–2.992)) and worse DFS

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(HR 1.788 (1.226–2.607)) and OS (HR 1.837 (1.135–2.973)). Other independent risk factors for intra-abdominal recurrence were an R1 resection (HR 2.616 (1.264–5.415)) and N2-stage (HR 2.096 (1.318–3.332)).

Conclusion

SSI following resection of a pT4N0-2M0 colon cancer is associated with an increased risk of intra-abdominal recurrence and worse survival. This finding supports the hypothesis that infection-based immunologic pathways play a role in colon cancer cell dissemination and outgrowth.

C56

INTRAPERITONEAL AND SYSTEMIC CHEMOTHERAPY FOR GASTRIC CANCER WITH PERITONEAL METASTASES

J.B.Y. So[1], D.Y.S. Chan[1], N.L.X. Syn[1], R. Yap[2], C.T. Neogh[2], J.N.S. Phua[1], E. Chen[1], J.S. Ho[2], H.L. Tan[2], N.Y.L. Ngoi[2], R. Sundar[2], C.S. Tan[2], C.E. Chee[2], A. Shabbir[1], W.P. Yong[2]

[1]National University Health System, Singapore - Singapore (Singapore), [2]National University Cancer Institute, Singapore - Singapore (Singapore)

Objectives

Peritoneal metastasis is common in gastric cancer. It is difficult to treat and is associated with grave prognosis. Studies have shown increased drug concentration in the peritoneal cavity when chemotherapy is administered via the intraperitoneal (IP) route. We had previously published early results on IP paclitaxel plus XELOX for such patients and now present our medium term data.

Methods

Patients with unresectable and/or recurrent gastric adenocarcinoma with peritoneal dissemination and/or positive peritoneal washing cytology, not previously-treated or received prior systemic therapy >180 days ago, and ECOG ≤ 2 are eligible. Patients were treated with 8 cycles of paclitaxel 40 mg/m^2 IP on days 1 and 8, oxaliplatin 100 mg/m^2 IV on day 1, and capecitabine 1000 mg/m^2 b.i.d. PO for 2 weeks followed by 1 week of rest. The primary endpoint is 1-year overall survival rate and the secondary endpoints are safety, response rate and peritoneal cytological response. Patients who subsequently have no distant metastases, with stable or reduced peritoneal disease and 2 consecutive negative peritoneal cytologies would then be eligible for conversion gastrectomy.

Results

34 patients have been enrolled, received at least one cycle at the time of reporting and are eligible for analysis. Median no. of cycles is 8 (range: 1–8) and median follow-up is 30.2 months. Median OS is 16.4 months (IQR: 10.1–27.2) and 1-year survival rate is 64.9% (95% CI: 45.5%–78.9%). Of 30 evaluable pts, 1 achieved CR (3.3%), 6 (20.0%) achieved PR, 16 (53.3%) achieved SD and 7 (23.3%) experienced PD. Peritoneal cytology turned negative in 17 of 32 (53.1%) pts. Severe (grade ≥ 3) AEs were neutropenia (N = 7), febrile neutropenia (N = 3), diarrhoea (N = 3), hand-foot syndrome (N = 2), bacterial peritonitis (N = 2) and hypokalaemia (N = 4) and tumour perforation (N = 1). One death occurred due to neutropenic sepsis. 8 patients had conversion gastrectomy with no additional morbidity, with a 1-year survival of 87.5% with a median OS of 18.8 months.

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Conclusion

XELOX+IP paclitaxel appears to be a well-tolerated and active regimen in gastric cancer with peritoneal metastases, and may offer survival benefits. Finally, conversion gastrectomy may be considered in pts with favourable response.

C57

ONCOLOGIC RESULTS OF CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) FOR GASTRIC CANCER WITH PERITONEAL CARCINOMATOSIS: MULTICENTER STUDY OF SPANISH GROUP OF PERITONEAL CANCER SURGERY (GECOP)

I. Manzanedo[1], F. Pereira[1], A. Gutiérrez-Calvo[2], R. Gómez-Sanz[2], F. Martínez-Regueira[3], G. Zozaya[3], Á. Casado-Adam[4], Á. Arjona[4], P. Cascales-Campos[5], J. Gil[5], X. Arteaga[6], A. García-Fadrique[7], Á. Serrano[1], E. Pérez-Viejo[1], A. López-García[2]

[1]Hospital Universitario de Fuenlabrada - Fuenlabrada (Spain), [2]Hospital Príncipe de Asturias - Alcalá De Henares (Spain), [3]Clínica Universitaria de Navarra - Pamplona (Spain), [4]Hospital Reina Sofía - Córdoba (Spain), [5]Hospital Virgen de la Arrixaca - Murcia (Spain), [6]Hospital Donosti - Donosti (Spain), [7]Instituto Valenciano de Oncología - Valencia (Spain)

Objectives

Gastric cancer with peritoneal carcinomatosis is considered a terminal stage of the disease, with a median survival of less than 6 months, and the standard treatment for these patients is systemic chemotherapy, palliative surgery and best supportive care. The use of multimodal treatments including cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) seems to be able to benefit this type of patients, although today it is still under discussion. Our aim is to analyze the survival results of these patients treated with systemic chemotherapy, CRS and HIPEC.

Methods

This is a retrospective multicenter study from a prospective national database of patients diagnosed on peritoneal carcinomatosis secondary to gastric cancer treated with CRS and HIPEC from June-2006 to October-2017.

Results

Eighty-eight patients from 7 Spanish Institutions were treated with CRS and HIPEC, with a median age of 53 years; 51% were women. Neoadjuvant systemic chemotherapy was administrated to 84 patients (95.5%) with a median cycles number of 4 (range 2–23). Median peritoneal cancer index (PCI) was 6 (range 0–30) and complete cytoreduction (CC-0) was achieved in 82 patients. Total gastrectomy was performed in 64 cases and subtotal gastrectomy in 14 patients. HIPEC was administrated in 85 cases with 4 different regimens (Cisplatin+Doxorubicin in 44 cases, Mitomycin-C +Cisplatin in 20 cases, Mitomycin-C in 10 cases and Oxaliplatin in 11 patients). Severe morbidity (Clavien-Dindo grade III-IV) was registered in 27 cases (30%) and 3 patients died for the procedure. Median hospital length stay was 14 days (range 4–93). Median follow-up was 19 months (range 2–103). Median disease-free survival (DFS) was 12 months with 1-year DFS of 46.1% and 3-year DFS of 21.7%. Median overall survival (OS) was 21 months with 1-year OS of 79.9% and 3-year DFS of 30.9%. After multivariate analysis, the extent of peritoneal disease (PCI ≥ 7) was identified as the only independent factor that influenced OS (HR: 2.52, 95%CI 1.36–4.68, p = 0.003).

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Conclusion

The multimodal treatment with systemic chemotherapy, CRS and HIPEC for gastric cancer with peritoneal carcinomatosis can improve the survival results in selected patients (with low PCI) and in referral centers.

C58

CYTOREDUCTIVE SURGERY VERSUS CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR SMALL BOWEL NEUROENDOCRINE TUMOR WITH PERITONEAL METASTASIS

F. Mercier[1], A. Pasquer[2], M. Gelli[3], E. Levine[4], L. Villeneuve[5], G. Poncet[6], T. Walter[6], O. Glehen[7]

[1]Hospices civils Lyon-Lyon Sud Hospital - Pierre Benite (France), [2]Hospices civils Lyon-Edouard Heriot Hospital - Lyon (France), [3]Gustave Roussy Institute - Villejuif (France), [4]Wake Forest University Baptist Medical Center - Winston Salem (United States), [5]Hospices Civils de Lyon- Lyon Sud Hospital - Pierre Benite (France), [6]Hospices Civils de Lyon-Edouard Heriot Hospital - Lyon (France), [7]Hospices Civils de Lyon-Lyon Sud Hospital - Pierre Benite (France)

Objectives

Background: Neuroendocrine tumor of the small bowel (sb-NET) are known to metastasize in the liver or retroperitoneal lymph node, often diagnosed at advance stage. Another frequent metastatic site is the peritoneum. The behavior and biology of neuroendocrine tumor is very peculiar with slow growing tumor who are resistant to chemotherapy associated with long survival even in metastatic state. In the past, peritoneal metastasis (PM) from sb-NET was neglected and considered not contributive to the patient prognostic and only patients with obstructive symptoms were treated. Aggressive combination of cytoreductive surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) are still debated in this indication.

Purpose: to assess the impact of HIPEC on survival and postoperative outcomes after complete CRS+HIPEC compared with CRS alone (CRSa).

Methods

From a multi-center international database (collaborative database of Peritoneal Surface Oncology Group International and BIG-RENAPE working groups), all patients who were treated for sb-NET and PM were identified. The “HIPEC group” represented patient treated with CRS and HIPEC and the “CRSa group” represented patient treated with CRS alone. Extension of the PM was assessed by the peritoneal cancer index (PCI) and cytoreductive effort was classified with the completeness of cytoreduction (CC) score.

Results

67 patients were identified in our databases, 31 without HIPEC and 36 with HIPEC. Mean follow-up was 46.4 months. Patients in the HIPEC group were significantly younger (58.1 vs 62.2 $p = 0.01$), with higher PCI (19 vs 7, $p = 0.009$) and had more CC-0/1 score (91.4% vs 51.9%, $p < 0.001$). Morbidity was higher in the HIPEC group with 50% of grade III or higher events compared to 3.4% ($p < 0.001$) and mortality rate was low at 3.1% in the HIPEC group. There was no difference between disease free survival of both groups ($p = 0.78$). The overall survival (OS) was not significantly different between both groups: the 5-years OS was 74.5% for the HIPEC group vs 91.6% for the CRSa group ($p = 0.316$).

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Conclusion

Despite a significantly higher PCI CRS and HIPEC achieved similar outcomes to CRS alone. However, the equivalent survival without achieving a CC0-1 resection calls into question how aggressive CRS should be in this setting. Morbidity is higher in the HIPEC group likely related to a more aggressive cytoreductive effort. More studies are needed to validate these findings and assess for prognosis factors.

C59

RESULTS OF CURATIVE STRATEGY IN PATIENTS WITH PERITONEAL AND EXTRAPERITONEAL METASTASES FROM COLORECTAL CANCER

I. Sourrouille, S. Derieux, M. Gelli, L. Benhaim, A. Mariani, M. Faron, C. Honoré, D. Elias, D. Goéré

Gustave Roussy - Villejuif (France)

Objectives

Curative treatment of peritoneal metastases from colorectal cancer (CRPM) relies on cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC). Benefits of this strategy remain uncertain when CRPM are associated with extraperitoneal metastases (EPM). The aim of this study was to compare outcomes of patients treated with CRS/HIPEC for CRPM, with or without EPM.

Methods

This study included 331 consecutive patients undergoing CRS/HIPEC for CRPM: 100 patients with EPM (EPM+) and 231 patients with isolated peritoneal carcinomatosis (EPM-). Patients with ovarian metastases and no other EPM were included in EPM- group (n = 75).

Results

EPM were mainly located to the liver (75%, n = 75) and retroperitoneal lymph nodes (31%, n = 31), and less frequently to the spleen (10%, n = 10), lung (4%, n = 4) or pleura (1%, n = 1). Thirty-nine patients (39%) in EPM+ had also ovarian metastases. Peritoneal carcinomatosis index (PCI) was similar in EPM- (8[4–14]) and EPM+ (8[4–14], $p = 0.964$), as were mortality (3% vs 4%, $p = 0.906$) and major morbidity rates (26% vs 33%, $p = 0.241$). Median overall survival (mOS) and disease-free survival were significantly higher in EPM- (56 vs 33 months, and 17 vs 10 months, $p < 0.01$). We highlighted 3 prognostic groups 1) EPM- with PCI < 10 (mOS 98 months), 2) EPM- with 10 < PCI < 15 (mOS 49 months) or EPM+ with PCI < 10 (mOS 52 months, $p = 0.534$), 3) EPM+ with 10 < PCI < 15 (mOS 29 months) or PCI > 15 whatever EPM (mOS 28 months, $p = 0.842$).

Conclusion

CRS/HIPEC seems to be feasible in patients with EPM, without increasing postoperative morbidity and mortality compared to patients without EPM. This curative strategy provides prolonged survival in selected with patients limited CRPM (PCI < 10).

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C60
TWO REGIMENS OF INTRAPERITONEAL CHEMOTHERAPY AFTER CYTOREDUCTIVE SURGERY IMPROVED SURVIVAL OF PATIENTS WITH COLORECTAL PERITONEAL METASTASES

S.Y. Park, J.S. Park, H.J. Kim, G.S. Choi, I.T. Woo

Department of Surgery, School of Medicine, Kyungpook National University - Daegu (Korea, Republic of)

Objectives

Hyperthermic intraperitoneal chemotherapy has been gaining popularity as intraperitoneal chemotherapy, even though there has been no robust evidence of the superiority in treatment of peritoneal metastasis compared with other types of intraperitoneal chemotherapy. The aim of this study was to investigate the survival benefit of the two types of intraperitoneal chemotherapy after cytoreductive surgery for patients with colorectal peritoneal metastasis.

Methods

An institutional database was retrospectively researched for all consecutive patients with colorectal peritoneal metastasis who were treated with cytoreductive surgery with or without intraperitoneal chemotherapy between October 1999 and June 2017. Patients who received palliative resection or who died postoperatively were excluded. Either early postoperative intraperitoneal chemotherapy (EPIC) or hyperthermic intraperitoneal chemotherapy (HIPEC) was used for intraperitoneal chemotherapy. The main endpoints were morbidity, and survival outcomes.

Results

The study included 138 patients; 49 patients underwent cytoreductive surgery only (surgery group), and 89 patients underwent cytoreductive surgery and intraperitoneal chemotherapy (IPCT group). The extent of peritoneal metastasis was significantly higher, and remnant overall metastatic disease was significantly greater in the IPCT group than in the surgery group. Median cancer-specific survival was 22.9 months in the surgery group, and 37.6 months in the IPCT group ($p = 0.005$). In patients who received complete resection of all metastatic disease, median progression-free survival was 12.2 months in the surgery group, and 16.8 months in the IPCT group ($p = 0.040$). Multivariate analysis revealed that tumor location (colon), lower peritoneal cancer index, no regional lymph node metastasis, and normal preoperative serums CA19-9 level, as well as intraperitoneal chemotherapy were independent better prognostic factors of cancer-specific survival. Intraperitoneal chemotherapy was also independently related to better progression-free survival and peritoneal progression-free survival. When patients in the IPCT group were compared according to the two types of intraperitoneal chemotherapy, there was no difference in the survival outcomes between EPIC and HIPEC.

Conclusion

Intraperitoneal chemotherapy was associated with improved survival outcomes compared with surgery alone, while we could not find different outcomes between the two types of intraperitoneal chemotherapy.

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C62
PROSPECTIVE COMPARATIVE ANALYSIS OF COMPLETE TOTAL PARIETAL PERITONECTOMY V/S SELECTIVE PERITONECTOMY WITH CRS+HIPEC IN PERITONEAL SURFACE MALIGNANCY - INDIAN SOCIETY OF PERITONEAL SURFACE MALIGNANCY (ISPSM) COLLABORATIVE GROUP STUDY

S.P. Somashekar, C. Rohit Kumar, S. Zaveri, K.R. Ashwin, Y. Ramya, A. Rauthan, V. Ahuja

Manipal Comphrensive Cancer Centre, Manipal Hospital - Bangalore (India)

Objectives

In spite of doing selective disease directed peritonectomy, fluoroscopic imaging & microscopy of remaining peritoneum has shown presence of disease that is not visible to naked eyes in peritoneal surface malignancy. The aim of this study was to assess the recurrence pattern, oncological outcomes (DFS & OS), morbidity & mortality of type of parietal peritonectomy with CRS & HIPEC.

Methods

Patients diagnosed with peritoneal surface malignancy from various diseases underwent complete parietal peritonectomy (CPP) or selective disease specific parietal peritonectomy (SPP) with CRS & HIPEC, done with Performer HT (RanD) machine. All data prospectively entered in the HIPEC registry was analyzed with main focus on pattern of recurrence, oncological outcomes, morbidity & mortality.

Results

Of the 163 cases, primary organ of origin were ovary, colorectal, stomach, mesothelioma (67.4%, 16.5%, 4.9%, 11%) respectively. Prior surgical score was 0,1,2,3 (101, 18, 38, 6 patient) respectively. 20 upfront, 94 interval and 49 recurrent cases. 70 & 93 patients underwent CPP & SPP respectively. CPP group had higher PCI (18.5 vs 8), longer duration of surgery (11 vs 9 hrs), more blood loss (1050 vs 600 ml) and increased hospital stay (14 vs 11) when compared to SPP group. The number of diaphragmatic resections, bowel resections, anastomosis and stoma were comparable in both group but CPP group had more splenectomy & multivisceral resections. Overall G3–G5 morbidity & mortality was comparable in both groups 39% v/s 32% & 5.7 v/s 4.5% respectively in CPP v/s SPP group. CPP group had increased intra-pleural & intra-abdominal collections which needed intervention. With a median follow up of 45 months, CPP group had a DFS & OS of 29 & 48 months respectively whereas SPP group had 20 & 43 months respectively. Most of the recurrences in CPP group were in lymph nodes 40%, liver 23% & extra abdominal (27%), peritoneal 10% Whereas in SPP most common site of recurrence were peritoneal (45%), nodal (30%) & extra-abdominal (25%).

Conclusion

Complete parietal peritonectomy lead to change in pattern of recurrence from peritoneal to systemic.CPP group had lower peritoneal recurrence & better DFS than SPP group with no significant morbidity or mortality. Complete parietal peritonectomy should be considered whenever doubtful of disease status specially in interval cytoreductive surgery & HIPEC group. A prospective randomized multi-institutional study needs to be designed for more evidence & better patient selection.

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C63
SURGIHONEY REACTIVE OXYGEN IN THE MANAGEMENT OF WOUNDS FOLLOWING CYTOREDUCTIVE SURGERY AND HIPEC

A. Pcolkins[1], A. Brandl[1], N. Battersby[1], M. Dryden[2], S. Nunn[1], F. Mohamed[1], S. Dayal[1], T. Cecil[1], B. Moran[1]

[1]Peritoneal Malignancy Institute - Basingstoke (United Kingdom), [2]Department of Microbiology, Hampshire Hospitals NHS Foundation Trust - Winchester (United Kingdom)

Objectives

Surgical site infection (SSI) after cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) remains challenging to manage increasing length of stay and reducing quality of life. An audit of wound complications at our institution showed a superficial wound dehiscence rate of 35% with iodine skin preparation alone. Both Chlorhexidine skin preparation and SurgiHoney Reactive Oxygen (SHRO), a novel antimicrobial therapy, highly active against Gram positive and negative bacteria have shown promise in reducing wound complications. We assessed the feasibility of SHRO application in patients undergoing CRS and HIPEC at our institution combined with Chlorhexidine skin preparation.

Methods

Prophylactic wound washout with saline alone or additional application of SHRO was performed in 41 consecutive patients undergoing CRS and HIPEC all of whom had chlorhexidine skin preparation. Anonymised wound photographs taken on day 10 post surgery were assessed by independent clinicians using ASEPSIS criteria. Secondary outcomes - wound infection, dehiscence, incision and drainage, and VAC dressing application - were obtained from medical records.

Results

Of 41 patients, 21 had prophylactic wound washout with saline alone and 20 with addition of SHRO. 5/41 patients (12%) developed superficial wound dehiscence and 2/41 (5%) required VAC dressing. No patient treated with SHRO required a VAC dressing compared with 2/21 in the saline only group.

Conclusion

There was a reduction in SSI rate for patients undergoing CRS and HIPEC compared with historical controls using a bundle of chlorhexidine skin preparation and SHRO /saline wash. Surgihoney is safe and feasible - and perhaps could be used in wounds at high risk of complications.

C64
OUTCOMES AFTER LAPAROSCOPIC CYTOREDUCTIVE SURGERY IN PATIENTS WITH LIMITED PERITONEAL METASTASIS OF COLORECTAL CANCER

S.Y. Park, J.S. Park, H.J. Kim, G.S. Choi, I.T. Woo, I.K. Park

Department of Surgery, School of Medicine, Kyungpook National University - Daegu (Korea, Republic of)

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Objectives

Laparoscopic approach has been rarely reported for colorectal cancer patients with peritoneal metastasis. The aim of this study was to investigate the safety and feasibility of laparoscopic cytoreductive surgery for colorectal cancer patients with limited peritoneal metastasis.

Methods

At our institution, laparoscopic surgery performed for colorectal cancer patients with peritoneal metastasis since December 2004. Patients were selected for laparoscopic cytoreductive surgery (LCRS) during explorative laparoscopy. Data for colorectal cancer patients with peritoneal cancer index (PCI) ≤ 10 were retrospectively identified from the institutional database. A total of 63 patients who underwent laparoscopic cytoreductive surgery (LCRS) or open cytoreductive surgery (OCRS). The outcomes, operative outcomes and follow-up oncologic outcomes were compared between LCRS group and OCRS group. The main endpoints were completeness of cytoreductive surgery (CCR), morbidity, cancer-specific survival, progression-free survival, and peritoneal progression-free survival.

Results

Overall, 21 patients underwent OCRS, and 42 patients underwent LCRS, of whom 6 patients (14.3%) required open conversion. The clinicopathological characteristics were not significantly different between the two groups except for a marginal difference in proportion to peritoneal carcinomatosis index (PCI > 5: 10 patients (47.6%) in the OCRS group, and 10 patients (23.8%) in the LCRS group; p = 0.056). CCR-0 was confirmed in 4 patients (100%) of the LCS group and 19 patients (91%) of the open group (p = 0.042). Operation time and postoperative morbidity rates were similar between the two groups. The hospital stay of the LCRS group was significantly shorter than that of the OCRS group (14.3 ± 7.3 vs. 20.2 ± 12.2; p = 0.019). Operative mortality occurred in one patient in each group. The 3-year cancer-specific survival rates were 66.3% in the OCRS, and 66.7% in the LCRS (p = 0.336). The 3-year disease-free survival rate was 32.6% in the OCRS group, and 38.72% in the LCRS (p = 0.175). The types of surgery (open versus laparoscopic) was not related to the cancer-specific survival in the univariate and multivariate analysis.

Conclusion

We performed exploratory laparoscopy for an optimal selection of patients for LCRS. Under the careful supervision by an experienced laparoscopic surgeon, LCRS was technically feasible and did not impair the efficacy of cytoreductive surgery in colorectal cancer patients with limited peritoneal metastasis.

C65

INCIDENCE AND RISK FACTORS OF NEUTROPENIA AFTER INTRAPERITONEAL CHEMOTHERAPY FOR ADVANCED COLORECTAL CANCER

S.Y. Park[1], J.S. Park[1], H.J. Kim[1], I.T. Woo[1], I.K. Park[1], G.S. Choi[1], J.G. Kim[2], B.W. Kang[2]

[1]Department of surgery, School of Medicine, Kyungpook National University - Daegu (Korea, Republic of), [2]Department of Oncology/Hematology, School of Medicine, Kyungpook National University - Daegu (Korea, Republic of)

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Objectives

Intraperitoneal chemotherapy with mitomycin C has a risk of neutropenia, which may exacerbate surgical complications and result in mortality. The aim of this study was to investigate the incidence and clinical risk factors for developing severe neutropenia after intraperitoneal chemotherapy for advanced colorectal cancer.

Methods

Data for colorectal cancer patients who received intraperitoneal chemotherapy from January 2005 to December 2017 were retrospectively identified from the institutional database. Patients received intraperitoneal chemotherapy for locally advanced tumor or peritoneal metastasis. Patients who underwent palliative surgery and intraperitoneal chemotherapy regimen without mitomycin C were excluded. Patient received early postoperative peritoneal chemotherapy (EPIC) or hyperthermic intraperitoneal chemotherapy (HIPEC). The clinical characteristics were compared between patients who had severe neutropenia (grade 3 or 4 according to the Common Terminology Criteria for Adverse Events v4.0) and patient who did not have grade 3/4 neutropenia. Binary logistic regression analysis was performed to define risk factors of grade 3/4 neutropenia.

Results

One hundred and nine patients were included in the analysis, of whom 30 patients (27.5%) developed grade 2 or more neutropenia and 22 patients (20.2%) developed grade 3/4 neutropenia. 36% of grade 3/4 neutropenia occurred between second and third week after intraperitoneal chemotherapy. Grade 3/4 surgical infectious complication occurred in 13.6% of patients with grade 3/4 neutropenia and 1.1% in patients without grade 3/4 neutropenia ($p = 0.005$). Two patients with grade 3/4 neutropenia died from postoperative infectious complication. Neutropenia occurred in 11.8% of patients with peritoneal cancer index (PCI) 0, 13.5% of patients with PCI ≤ 5, and 34.2% of patients with PCI > 5 ($p = 0.028$). Multivariate logistic regression revealed that body mass index [odds ratio (OR) = 0.845; 95% confidence interval (CI) 0.718–0.994] and PCI > 5 [OR = 4.200; 95% CI 1.185–14.884)] were independently associated with developing grade3/4 neutropenia.

Conclusion

Neutropenia was significantly related to the serious infectious complication after intraperitoneal chemotherapy. Considering the time to occurrence of neutropenia and postoperative adjuvant chemotherapy, the changes of leukocyte profile should be carefully followed between 1–3 weeks after intraperitoneal chemotherapy, especially in patients with extended peritoneal metastasis (PCI > 5).

C66

CHEMOTHERAPY DRUGS VERSUS POSTOPERATIVE MORBIDTY IN HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR PERITONEAL SURFACE MALIGNANCIES: INDIAN SOCIETY FOR PERITONEAL SURFACE MALIGNANCY COLLABORATION STUDY

A. Kr, S. Sp, S. Zaveri S, R. Kumar, R. Yetahdka, A. Rauthan

Manipal hospital, Bengaluru - Bangalore (India)

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Objectives

The morbidity associated with cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) is due to the synergistic effect of major cytoreduction, effect of hyperthermia and the cytotoxic agents used for HIPEC.

Methods

This study was done to analyse the cytotoxic agents used and their relation to the postoperative morbidity in patients undergoing CRS-HIPEC for peritoneal surface malignancy (PSM) in Indian set up. Patient with PSM, underwent CRS-HIPEC as per the institutional protocol. Patients were stratified as per the chemo drug use during HIPEC & perioperative outcome were documented.

Results

Total of 163 patients underwent CRS-HIPEC for PSM and majority had peritoneal carcinomatosis secondary to ovarian primary (67.4%). Others were of colorectal, appendicular, gastric primary and rarer tumors. Cisplatin was the most common drug used: as alone (57.05%) or as combination with Adriamycin (12.88%). Mitomycin-C (MMC) was used in 33 patients and bidirectional oxaliplatin in 16 patients. The overall severe morbidity (Grade 3–5) in the cohort was 44.8% and minor was 74%. Electrolyte abnormality was the most common minor complication observed (73.5%) and the most common major complication was surgical (25%). Adriamycin combination patient had a G3 or more morbidity of 61.9%. The frequency of severe morbidity were 61.9%, 54.5%, 38.7% and 37.5% for Adriamycin+ cisplatin, MMC, cisplatin alone and oxaliplatin respectively. All the major complications were highest in the group who received Adriamycin combination. HIPEC with platinum agents was associated with a higher rate of acute renal impairment and oxaliplatin was associated with higher rates of post-operative bleeding. Rates of other complications did not differ significantly between the groups receiving different HIPEC regimens.

Conclusion

The impact of cytotoxic agents in patient undergoing HIPEC. In this study, it was seen clearly that tolerance to Adriamycin combination regimen in Indian patient is poor and can have significant impact over on the continuation of further adjuvant therapy.

C67

DELTA PERITONEAL CANCER INDEX (∆PCI): A NEW DYNAMIC PROGNOSTIC PARAMETER FOR SURVIVAL IN PATIENTS WITH PERITONEAL CARCINOMATOSIS FROM COLORECTAL CANCER

J. Hentzen, W. Van Der Plas, H. Kuipers, S. Ramcharan, L. Been, F. Hoogwater, R. Van Ginkel, G. Van Dam, P. Hemmer, S. Kruijff

University Medical Centre Groningen - Groningen (Netherlands)

Objectives

The Peritoneal Cancer Index (PCI) is a score at single time-point which is often used in selecting patients with peritoneal carcinomatosis from colorectal cancer (pm-CRC) for complete cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) and is also a strong prognostic factor for survival. Unfortunately, the static PCI does not include disease progression. Therefore, we aimed to identify the impact of an increase in PCI (∆PCI) from diagnostic laparoscopy (DLS) to CRS and HIPEC on survival in patients with pm-CRC.

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Methods

Patients undergoing DLS and attempt to CRS and HIPEC between 2011 and 2018 were included retrospectively. Patients were divided into three subgroups: ΔPCI 0–3, ΔPCI 4–9 and ΔPCI ≥ 10. Primary outcome was overall survival (OS). Kaplan-Meier analysis was used to compare OS between the ΔPCI groups. A proportional hazard analysis was performed to examine the association of ΔPCI with the risk of death. To adjust for potential confounders, a multivariate Cox regression analysis was used.

Results

Eighty-one patients with histology proven pm-CRC (ΔPCI 0–3 n = 31, ΔPCI 4–9 n = 35 and ΔPCI ≥ 10 n = 15) and a median follow up of 17 months (8–33) were analyzed. The median PCI at DLS was 4 (interquartile range, 2–11) and increased to 11 (6–18) at the time of CRS and HIPEC (P < 0.001). Median time from DLS to CRS and HIPEC was 5 (3–9) weeks and was comparable between the groups (P = 0.44). Fourteen (17.3%) patients had an open-close procedure which was equally distributed among the three groups (P = 0.31). OS in the ΔPCI 0–3, ΔPCI 4–9 and ΔPCI ≥ 10 was 41, 27 and 14 months respectively (P = 0.011). In a multivariate regression analysis, including PCI at DLS and resection status, ΔPCI remained an independent risk factor for OS: ΔPCI 4–9 hazard ratio (HR) 3.0 (95% confidence interval [CI] 1.2–7.6, P = 0.023) and ΔPCI ≥ 10 HR 4.4 (95% CI 1.5–13.3, P = 0.009).

Conclusion

ΔPCI appears to be an independent prognostic factor for OS and potentially reflects on a more aggressive tumor biology and disease progression in patients with pm-CRC. HIPEC surgeons should be aware of a ΔPCI related worse prognosis and when confronted with a high ΔPCI reconsider CRS and HIPEC.

C68

THE IMPACT OF SYNCHRONOUS VERSUS METACHRONOUS PERITONITIS CARCINOMATOSA ON OVERALL- AND DISEASE-FREE SURVIVAL IN COLORECTAL PATIENTS SCHEDULED FOR

J. Hentzen[1], K. Rovers[2], H. Kuipers[1], W. Van Der Plas[1], L. Been[1], F. Hoogwater[1], R. Van Ginkel[1], G. Van Dam[1], P. Hemmer[1], I. De Hingh[2], S. Kruijff[1]

[1]University Medical Centre Groningen - Groningen (Netherlands), [2]Catharina Hospital - Eindhoven (Netherlands)

Objectives

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) has significantly improved overall survival of patients with peritonitis carcinomatosa (PC) of colorectal origin. Whether development of synchronous PC (sPC) or metachronous PC (mPC) - early or late onset - has a different impact on survival is often subject of debate in multidisciplinary meetings. Therefore, we aimed to identify the impact of synchronous versus early or late metachronous PC on overall survival (OS) and disease-free survival (DFS).

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Methods

Patients with PC of colorectal origin scheduled for CRS and HIPEC between 2006 and 2018 in two specialized HIPEC centers in the Netherlands were included prospectively. Patient data were compared between patients with sPC and mPC on OS and DFS using Kaplan-Meier analysis and proportional hazard analysis. To adjust for potential confounders, including Peritoneal Carcinoma Index (PCI) and signet cell histology, a multivariate Cox regression analysis was used.

Results

Four hundred eighty-six patients (sPC n = 254 and mPC n = 232) were included. OS was comparable within the two groups (34 versus 26 months, respectively; p = 0.11). DFS in the mPC group was 10 (8–12) months compared to 15 (11–19) months in the sPC group (p < 0.001). In a multivariate regression analysis mPC remained an independent risk factor for decreased DFS (HR: 1.6, 95% confidence interval 1.1–2.2, p = 0.009). Subanalysis of the mPC group showed no difference in DFS between patients who developed PC within 12 months, between 12 and 24 months and after more than two years of primary surgery (11, 8 and 11 months respectively, p = 0.50).

Conclusion

Patients with mPC of colorectal origin have a significant shorter DFS compared to sPC. There was no difference between patients presenting with early or late PC. These findings are relevant for preoperative decision making and future research needs to focus on the early detection of PC.

C69

PERITONEAL AND EXTRAPERITONEAL RELAPSE AFTER PREVIOUS CURATIVE TREATMENT OF PERITONEAL METASTASES FROM COLORECTAL CANCER: WHAT SURVIVAL CAN WE EXPECT?

M. Gelli, J.F.L. Huguenin, T. De Baere, L. Benhaim, A. Mariani, V. Boige, D. Malka, M. Ducreux, D. Elias, D. Goéré

Gustave Roussy - Villejuif (France)

Objectives

Over the last 20 years, complete cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) dramatically increased survival of patients with colorectal peritoneal metastases (CRPM). However, despite better knowledge of the disease, around 70% of patients relapse after CRS with HIPEC. This study was designed to analyze the pattern of recurrence and the outcomes of different treatment modalities.

Methods

Patients relapsing after CRS plus HIPEC for CRPM were selected from a prospective database. The impact of iterative curative-intent treatments was analyzed using Kaplan-Meier estimates and multivariate Cox regression models.

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Results

Between April 1993 and December 2014, 190 of 274 (69%) patients previously treated by CRS plus HIPEC developed relapse, as an isolated peritoneal recurrence (31%), isolated distant recurrence (35%), or multisite recurrence (34%). The curative-intent treatment rate was 48% for isolated peritoneal recurrences, 49% for isolated distant recurrences and 22% for multisite recurrences ($p = 0.002$). From the diagnosis of relapse, three- and five-year overall survival were 77% and 46% after curative-intent treatment and 14% and 4.7% after non-curative treatment, with median survival of 59.7 and 18.3 months (log-rank $p < 0.0001$), respectively. Regression analysis identified the initial extent of CRPM (hazard ratio [HR] 2.25; $p < 0.0001$), iterative curative-intent treatment (HR 0.22; $p < 0.0001$) and disease-free interval (HR 1.77; $p = 0.01$) as independent predictors of prolonged survival.

Conclusion

Iterative curative-intent treatment can be performed in up to 40% of patients with relapse after CRS and HIPEC for CRPM, and is associated with prolonged survival in selected patients.

C70

PATHOLOGICAL N2 STATUS IS PREDICTIVE OF A HIGH INCIDENCE OF PERITONEAL METASTASES IN PATIENTS UNDERGOING CURATIVE SURGICAL TREATMENT FOR COLORECTAL CANCER-EXPERIENCE FROM AN INDIAN TERTIARY CARE INSTITUTION

R. Bhamre[1], A. Bhatt[2], J. Rohila[1], V. Kalikar[3], A. Desouza[1], A. Saklani[1]

[1]Tata Memorial Hospital - Mumbai (India), [2]Zydus Hospital - Ahmedabad (India), [3]Zen Hospital - Mumbai (India)

Objectives

To determine the incidence and clinical behavior of peritoneal metastases (PM) in patients with colorectal cancer undergoing potentially curative surgery and having extensive loco-regional lymph node involvement (pathological N2) and compare it with that in patients with serosal involvement (T4) (a known risk factor for developing PM).

To compare the survival in patients with and without PM.

Methods

A retrospective analysis of a prospectively maintained database was performed. All patients with pathological T stage T4 and/or nodal status N2 were included in the analysis. The diagnostic criteria were finding of PM during surgical exploration with biopsy confirmation, imaging features suggestive of PM and/or the presence of ascites, ovarian metastases and omental deposits. All patients were followed up till death from any cause.

Results

214 patients treated between May 2010 and October 2015 were included in the analysis. Of these 110 (51.4%) patients had T4 tumors and 131 (61.2%) had N2 tumors (27 patients with T4N2 tumors were included in both groups). 17.2% patients with T4 tumors and 20.2% patients with N2 tumors developed PM ($p = 0.53$). Non-peritoneal metastases developed in 19.0% of all patients with T4 tumors and 37.5% with N2 tumors.

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The median time to detection of PM was 16.2 months and 12.2 months for T4 and N2 tumors respectively. The PM were symptomatic in 36.8% of T4 and 55.5% of N2 tumors (p = 0.21). The PM were isolated in 68.4% patients with T4 tumors and in 51.8% of the patients with N2 tumors.

In patients with N2 disease, there was a higher incidence of PM in those with poorly differentiated tumors (p < 0.01), positive surgical margins (p = 0.02), colonic tumors versus rectal tumors (p = <0.01) and right sided tumors. (p = 0.01).

The median OS was 39.2 months and not reached for colonic tumors with and without PM (p = 0.027) and 27.9 months and 61.9 months for rectal tumors with and without PM respectively (p < 0.01). The patients without PM included those with liver and lung only metastases and those with multiple non-peritoneal sites of metastases.

Conclusion

Pathological N2 status is a risk factor for developing PM. The incidence of PM in these patients is similar to that with T4 disease. The peak incidence is reached at 18 months due to irregular follow-up in our patients with nearly 50% presenting with symptoms. Nearly 50% of these patients have isolated PM. Preventive and second look strategies should include this subgroup of patients.

C71

IMPACT OF THE PCI ON OUTCOMES OF CYTOREDUCTIVE SURGERY AND HIPEC IN PATIENTS WITH MUCINOUS COLORECTAL PERITONEAL METASTASES- A REPORT FROM THE INDIAN HIPEC REGISTRY

A. Bhatt[1], P. Kammer[2], S. Zaveri[3], D. Damodaran[4], M. Ray[5], N. Katdar[6], S. Sinukumar[7], R. Seshadri[8], S. Mehta[9]

[1]Zydus Hospital - Ahmedabad (India), [2]Global hospital - Hyderabad (India), [3]Manipal Hospital - Bangalore (India), [4]MVR Cancer Institute and Research Center - Calicut (India), [5]All India Institute of Medical Sciences - New Delhi (India), [6]SL Raheja Hospital - Mumbai (India), [7]Jehangir Hospital - Pune (India), [8]Cancer Institute (WIA) - Chennai (India), [9]Saifee Hospital - Mumbai (India)

Objectives

To evaluate clinical outcomes in patients with mucinous versus non-mucinous colorectal peritoneal metastases (PM) undergoing cytoreductive surgery (CRS) and HIPEC.
To determine the impact of PCI on survival in these patients.

Methods

A retrospective analysis of patients enrolled in the Indian HIPEC registry treated between Jan 2013 and September 2017 was performed

The patient and disease characteristics, perioperative and survival outcomes were evaluated and compared with patients with non-mucinous tumors treated during the same period.

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Results

There were 25 patients with mucinous and 43 with non-mucinous tumors. In the mucinous group, there were 3 rectal tumors and 22 colonic tumors of which 17 were right sided and 5 left sided. The proportion of right sided tumors ($p = 0.02$) and ovarian metastases ($p = 0.01$) was higher in the mucinous group ($p = 0.02$). The mucinous group had a median PCI was 13 [range 4–35] compared to 8 [range 3–27] in the non-mucinous group and more patients with a PCI >12 ($p = 0.01$). All patients in both groups except 1 in the mucinous group had a complete cytoreduction (CC-0/1). HIPEC was performed in 92% in the mucinous and 90.6% in the non-mucinous group ($p = 0.85$). 88% in the mucinous and 88.3% in the non-mucinous group received 6 months of perioperative chemotherapy. The 90-day grade 3–4 morbidity was higher in the non-mucinous group ($p < 0.001$) but the 90-day mortality was the same (1 patient in the mucinous and 2 in the non-mucinous group; $p = 0.85$).

The median disease free survival (DFS) was 12 months in both groups and the median overall survival (OS) was 26 months for mucinous and 20 months for non-mucinous tumors ($p = 0.51$). The median OS was longer in both groups for PCI < 12 compared to PCI > 12 ($p < 0.001$ for nonmucinous and $p = 0.08$ for mucinous tumors). It was longer in patients with mucinous tumors with a PCI > 12 compared to non-mucinous tumors though not significantly (19 versus 11 months; $p = 0.31$). Mucinous tumors with PCI > 20 had a shorter DFS ($p = 0.016$) and OS ($p = <0.001$) compared to PCI > 20. A PCI < 20 [hazard ratio (HR)-0.109; 95% confidence interval(CI) 0.021–0.570; $p < 0.001$] was the only independent predictor of a longer OS.

Conclusion

Patient with mucinous colorectal PM with PCI > 20 had a significantly inferior DFS and OS compared to patients with PCI < 20. Evaluation of larger series is needed to determine the prognostic factors for patients with mucinous colorectal PM undergoing CRS and HIPEC and to determine its benefit in patients with extensive disease.

C72

ASSESSING THE HERITAGE OF PERITONEAL METASTASIS OF COLORECTAL ORIGIN: DOES THE LOCATION OF THE INITIAL PRIMARY TUMOUR HAVE AN EFFECT ON THE DISEASE SEVERITY AND THE OUTCOME OF CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY?

Z.Z. Yong[1], G.H.C. Tan[2], M.C.C. Teo[2]

[1]Department of General Surgery, Singapore General Hospital (Singapore), [2]Division of Surgical Oncology, National Cancer Centre Singapore (Singapore)

Objectives

There are increasing data to suggest distinct biological heterogeneity of tumours arising from different locations of the colon. As a result, many studies have reported varying outcomes of the same treatment on colorectal tumours of arising from different locations. This has not been investigated in patients with peritoneal metastases (pCRC) undergoing cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). This study aims to investigate if the locality of the primary tumour affects the efficacy of CRS and HIPEC for pCRC.

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Methods

A retrospective analysis of patients who underwent CRS and HIPEC at the National Cancer Centre Singapore from February 2003 to February 2018 was performed. A total of 101 pCRC cases were included in this study. Patients were grouped according to their primary tumour location, and the Peritoneal Carcinomatosis Index (PCI) score, completeness of cytoreduction score (CCS), intra-operative complications, post-operative recovery and overall survival (OS) were compared.

Results

Between the right-sided, left-sided and rectal tumour groups, the median PCI score were comparable (9 vs. 7 vs. 6, p = 0.87), with the majority of patients achieving complete cytoreduction (i.e. CCS = 0) (97% vs. 100% vs. 100%, p = 0.35). Intra-operatively, the median blood loss (750 ml vs. 800 ml vs. 900 ml p = 0.74) and complications encountered (9.1% vs. 9.8% vs. 0%, p = 0.41) were in proportion amongst the different groups. Post-operatively, the median days spent in the intensive care unit (1 vs. 1 vs. 1, p = 0.39), median days taken to tolerate full feeds (5 vs. 5 vs. 5, p = 0.35), and median days of hospitalization (12 vs. 12 vs. 12, p = 0.82) were also consistent between the different groups. There was no difference in recurrence (49% vs. 53% vs. 53%, p = 0.91), and the median time to recurrence in months (11 vs. 12 vs. 6, p = 0.49). Lastly, the 1-year OS (78% vs. 90% vs. 100%, p = 0.16), 3-year OS (46% vs. 52% vs. 50%, p = 0.93) and 5-year OS (20% vs. 11% vs. 16%, p = 0.80) between the right-sided, left-sided and rectal tumour groups were all comparable.

Conclusion

The locality of the colorectal tumour was not found to be a prognostic factor, with outcomes of CRS and HIPEC being similar in all tumours that arose from different locations in the colon.

C73

PREOPERATIVE SYSTEMIC CHEMOTHERAPY IN PATIENTS WITH PMCA OF APPENDICEAL ORIGIN TREATED WITH CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY

P. Ledakis, M.C. King, C. Munoz, V. Gushchin, M. Sittig, A. Sardi

Mercy Medical Center - Baltimore (United States)

Objectives

The role of systemic chemotherapy (SC) before cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) for patients with peritoneal mucinous carcinomatosis (PMCA) is controversial. This study explores the effect of SC prior to CRS/HIPEC on outcomes in patients with PMCA of appendiceal origin (AO).

Methods

A retrospective review of a prospective database of CRS/HIPEC patients from 1998–2017 was conducted. Patients with histopathology of PMCA of AO with or without signet ring cells (PMCA-S) were identified. Patients who had extensive prior debulking surgeries (>5 regions) or received >2 lines of prior SC were excluded from analysis. Perioperative variables were analyzed. Survival was estimated using the Kaplan-Meier method.

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Results

Patients with PMCA of AO (n = 140) were identified with median follow up of 3 years. Sixty-four (46%) patients received prior SC (G1) and 76 (54%) did not receive prior SC (G2). SC included 5-FU, oxaliplatin, irinotecan, and bevacizumab per colon cancer regimens. Groups were balanced with respect to age, gender, lymph node status, complete cytoreduction rate, length of surgery, burden of disease, hospital stay, grade III/IV complications, and postoperative SC. G1 had more patients with PMCA-S, high-grade histology (HG), prior surgeries (>1 region), and longer time from diagnosis to surgery (median: 6 vs 2 months, $p < 0.001$). Median overall survival (mOS) was 40 vs 86 months for G1 and G2, respectively ($p = 0.006$). Median progression free survival (mPFS) was 23 vs 43 months for G1 and G2, respectively ($p = 0.01$). For PMCA-S (36 G1 & 25 G2), mOS was 25 vs 39 months and mPFS was 17 vs 29 months for G1 and G2, respectively ($p = 0.188$ & $p = 0.063$). Prior SC did not impact OS or PFS in non-signet ring PMCA (28 G1 & 51 G2) ($p = 0.639$ & $p = 0.512$). In HG (49 G1 & 36 G2), mOS was 38 vs 56 months and mPFS was 18 vs 29 months in G1 and G2, respectively ($p = 0.199$ & 0.082). In low-grade histology (LG) (10 G1 & 35 G2), prior SC did not impact OS or PFS ($p = 0.721$ & $p = 0.253$).

Conclusion

Prior SC was not associated with less disease burden, better complete cytoreduction rates, or improved clinical outcomes in patients with PMCA, regardless of histopathologic subtype (non-signet ring PMCA, PMCA-S, HG or LG). Time to surgery was significantly longer in patients who received prior SC across all subgroups and appears to adversely affect survival. Traditional SC agents are not effective in PMCA; thus, other regimens should be explored.

C74

QUALITY OF PRIMARY SURGICAL RESECTION IS A CRITICAL PROGNOSTIC FACTOR IN PATIENTS WITH CYTOREDUCTIVE SURGERY AND HIPEC FOR PERITONEAL CARCINOMATOSIS FROM COLORECTAL CANCER

M. Ströhlein, S. Seefeldt, P. Thomaidis, M. Heiss

Cologne Merheim Medical Center, Witten, Herdecke University - Cologne (Germany)

Objectives

Cytoreductive surgery (CRS) with CC-0 resection and Hyperthermic chemoperfusion (HIPEC) is the standard treatment for colon cancer and resectable peritoneal carcinomatosis (PC). Despite successful CC-0 resection during CRS, several patients suffer from early cancer relapse. A possible explanation may be patient´s history before CRS, as PC is often found as a surprising diagnosis during elective surgery or emergency surgery, when HIPEC treatment is not available, and complete cytoreduction is not performed. Therefore, the role of the quality of primary surgery remains unclear: Aim of study was to investigate the prognostic influence of primary CC-0 vs. incomplete R2 resection, emergency surgery, inductive chemotherapy, and second look laparotomy with CRS and HIPEC.

Methods

We investigated a series of 51 patients with peritoneal metastasis of colon cancer, who all had complete cytoreduction (CC-0) and HIPEC either by one step surgery (15) or by a second look concept (36). Overall survival, PCI, quality of primary surgery by primary R-status, emergency surgery, ascites, ileus, extent of PC and systemic chemotherapy were assessed. Log-rank analysis, student´s t-test and multivariate regression analysis were used for statistical calculation.

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Results

Primary R2 resection vs. complete resection, (18.6 vs. 49.6 months, p = 0.001), high PCI (p = 0.03) and ileus (26.4 vs. 55.6 months, p = 0.007) were found to be associated with impaired survival, whereas ascites, emergency surgery, primary vs. secondary CRS+HIPEC and inductive chemotherapy had no significant effect. Multivariate regression analysis showed primary incomplete R2 resection vs. complete resection to be an independent prognostic parameter (p = 0.003).

Conclusion

The quality of primary surgery in terms of complete cancer resection is a substantial significant prognostic factor in patients with PC from colon cancer. Secondary CC-0 cytoreduction and HIPEC after incomplete cancer resection are not able to compensate primary resection failure. Therefore, complete cancer resection with all peritoneal metastases should be mandatory in patients with first and previously unknown diagnosis of PC during elective of emergency surgery. When complete cancer resection is not manageable, incomplete resection is not favorable and patients should be transferred to specialized centers.

C75
BLADDER RESECTION AND HIPEC

V. Verwaal[1], K. Speeten[2], I. De Hingh[3], S. S.p.[4], M. Møller[5], D. Morris[6], A. Mehta[7], O. Glehen[8], P. Sugarbaker[9]

[1]Aarhus University Hospital - Aarhus (Denmark), [2]ZOL - Genk (Belgium), [3]Catharina Hospital - Eindhoven (Netherlands), [4]Manipal Comprehensive Cancer Centre - Bangalore (India), [5]Aarhus University Hospital - Aarhus (Denmark), [6]St George Hospital - Sydney (Austria), [7]St Marks Hospital - London (United Kingdom), [8]Centre Hospitalier Lyon, - Pierre Bénite (France), [9]MedStar Washington Hospital Centre - Washington (United States)

Objectives

The basic limitation of CRS and HIPEC has always been resectability of the peritoneal metastasis. On the other side come are there patients which have peritoneal metastasis together with advanced disease in the pelvis. In these patients is the resectability determined rather by the pelvic disease then by the peritoneal metastasis. In this study we look at patients who underwent a total exenteration together with CRS and HIPEC in HIPEC centres though out the world.

Methods

22 patients from different hospital and international data bases were identified to have undergone an exenteration together with CRT and HIPEC for various diseases though out the world. Basic data together with disease, data on neo adjuvant treatment and adjuvant treatment were collected. Details about the CRS and HIPEC with focus on resections and reconstruction were also collected. Finally, were data on post-operative complication and follow-up collected.

Results

Out of the 23 patients 11 were male and 12 were female with a mean age of 59 years. The indication for HIPEC with bladder resections were Colorectal cancer 16, appendix cancer in 2, PMP in 1; Ovary cancer in 3 and small bowel cancer in one patient. 9 patients were treated for synchronic and 14 for meta chronic disease. Median PCI was 7 (range 0–17). Of the 23 patients had 20 a bricker bladder two a colon conduit

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and one a redo bricker. 8 patients had complication grade 3 or more and 4 patients were re-operated. 6 patients had electrolyte disturbances, 3 grade 1, 2 grade 2 and 1 grade 3. One patient had a leakage of the bricker bladder. There was no treatment related mortality. The median survival time of the whole group was 44 months, of those with Colorectal origin of the disease it was 15 months.

Conclusion

The combination of CRS+HIPEC and bladder resection is do-able but lead to certain morbidity. On the other side is the median survival reasonable in this small series.

C76

COMPARISON OF PROGNOSTIC VALUE OF PSOGI AND WHO PATHOLOGIC CLASSIFICATIONS OF PATIENTS WITH APPENDICEAL MUCINOUS NEOPLASMS AND ASSOCIATED PSEUDOMYXOMA PERITONEI

S. Er[1], C. Yüksel[2], U.F. Turan[1], S. Özden[1], Ö. Yalkin[2], S. Güresci[3], M. Tez[3], A.E. Ünal[2]

[1]The Health Sciences University, Ankara Numune Training and Research Hospital, Department of Surgery - Ankara (Turkey), [2]Ankara University, Faculty of Medicine, Department of Surgical Oncology - Ankara (Turkey), [3]The Health Sciences University, Ankara Numune Training and Research Hospital, Department of Pathology - Ankara (Turkey)

Objectives

The aim of this study was to evaluate the repeatability and prognostic significance of pathological classifications which was recently recommended by Peritoneal Surface Oncology Group International (PSOGI) and the World Health Organization (WHO).

Methods

We retrospectively reviewed 52 appendiceal mucinous neoplasia and PMP patients who underwent surgical treatment from 2010 to 2018 at our clinics. According to PSOGI, primary appendiceal tumors were classified as low, and high grade appendiceal mucinous neoplasia (LG-AMN, HG-AMN), mucinous adeno cancer (MAC), and signet-ring cells (SRC) cancer. Peritoneal disease was classified as only mucin, low, and high grade peritoneal disease (LG-PD, HG-PD), and SRC cancer. According to WHO, primary appendiceal tumors was classified as LG-AMN and MAC. However, in the presence of peritoneal disease there are only two grade as LG-PD and HG-PD.

Results

The median age of patients were 61 (30–80) years. 25 (48%) were male and 27 (52%) were female. After surgery, median follow-up time was 16 (0–91) months. According to PSOGI, 23 (44%) patients were LG-AMN, 1 (3%) was HG-AMN and 28 (53%) were MAK, whereas SRC and only mucin subgroup were not found. According to WHO, 23 (44%) of appendiceal limited patients were LG-AMN and 6 (10%) were MAC. However, according to the presence of peritoneal disease, 1 (4%) patient was LG-PD and 22 (42%) were HG-PD. For surgical treatment; 22 (42%), 20 (38%), and 10 (20%) patients underwent SRC-HIPEK, right hemicolectomy, and only appendectomy respectively. In Kaplan-Meier analysis; PSOGI and WHO classifications were statistically significant (p: 0.17, p: 0.16, respectively), in prediction of overall survival. In the ROC analysis, area under curve (AUC) was 0.709 (95% CI 0,561–0,857) and p: 0.15 for PSOGI. AUC for WHO was found to be 0.710 (95% CI 0.562–0.858) and p: 0.15.

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Conclusion

In our study, in the presence of appendiceal mucinous neoplasia or peritoneal disease, the PSOGI and WHO classification has shown to be equally meaningful in prediction overall survival.

C77

TREATMENT AND SURVIVAL AMONG DANISH PATIENTS WITH COLORECTAL SYNCHRONOUS PERITONEAL METASTASES

S. Ravn[1], C.F. Christiansen[2], U. Heide-Joergensen[2], R.H. Hagemann-Madsen[3], V.J. Verwaal[1], L.H. Iversen[1]

[1]Department of Surgery, Colorectal Surgical Unit, Aarhus University Hospital - Aarhus (Denmark), [2]Department of Clinical Epidemiology, Aarhus University Hospital - Aarhus (Denmark), [3]Department of Pathology, Lillebaelt Hospital - Vejle (Denmark)

Objectives

To describe treatment and survival among patients with synchronous peritoneal metastases (S-PM) from colorectal cancer (CRC).

Methods

The study was performed as a population-based study of Danish patients diagnosed with S-PM between 2014–2015 and followed until January 2017 (follow-up in June 2018 is planned). Patients with S-PM were identified using the Danish Colorectal Cancer Group database, the Danish National Patient Registry and the Danish Pathology Registry. The same registries were used to identify treatment characteristics within 180 days after CRC diagnosis. Treatment was categorized into 4 groups based on specific algorithms. Patients were excluded if another cancer was recorded within 5 years prior to CRC diagnosis.

One- and 2-year survival rates were computed using Kaplan-Meier survival analysis for patients who had survived 180 days after CRC diagnosis.

Results

Among 468 patients with S-PM, 102 (22%) received ‘no treatment’, 210 (45%) received ‘alleviating surgery and/or systemic chemotherapy’, 127 (27%) had a ‘colonic/rectal resection of the primary tumour±systemic chemotherapy’ and 29 (6%) received ‘cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC)’.

Preliminary estimates show 1- and 2-year crude survival rates of 53% (95 CI:29;72) and 24% (95 CI:8;45) when receiving ‘no treatment’, 65% (95 CI:57;73) and 24% (95 CI:17;33) when ‘alleviated with surgery and/or systemic chemotherapy’, 69% (95 CI:59;77) and 36% (95 CI:26;46) after a ‘colonic/rectal tumour resection±systemic chemotherapy’, and 100% (95 CI: NA) and 95% (95 CI:68;99) when treated with ‘CRS+HIPEC’.

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Conclusion

There is a large difference in the treatment of patients with S-PM even though CRS+HIPEC is a well-known treatment option with favourable outcome. One can expect that the population-based survival will increase once CRS+HIPEC is performed in a larger proportion of these patients.

C78

RISK FACTORS FOR METACHRONOUS PERITONEAL METASTASES: A NATIONWIDE POPULATION-BASED COHORT STUDY OF DANISH COLORECTAL CANCER PATIENTS

S. Ravn[1], C.F. Christiansen[2], U. Heide-Joergensen[2], R.H. Hagemann-Ma[3], V.J. Verwaal[1], L.H. Iversen[1]

[1]Department of Surgery, Colorectal Surgical Unit, Aarhus University Hospital - Aarhus (Denmark), [2]Department of Clinical Epidemiology, Aarhus University Hospital - Aarhus (Denmark), [3]Department of Pathology, Lillebaelt Hospital - Vejle (Denmark)

Objectives

To identify risk factors for metachronous peritoneal metastases (M-PM) after curative colorectal cancer (CRC) surgery.

Methods

This nationwide register-based cohort study included all Danish CRC patients from 2006–2015. M-PM was defined as PM diagnosed ≥180 days after CRC diagnosis and identified using the Danish Colorectal Cancer Group database, The Danish Pathology Registry and The Danish National Patient Registry.

Patients were excluded if another cancer was recorded within 5 years prior to CRC diagnosis, if CRC treatment was non-curative.

Potential predictors of M-PM were estimated by a multivariable absolute risk regression, treating death and other cancer as competing risks. One and 3-year risk differences (RD) are presented as the absolute difference between groups.

Results

In total, 22,585 patients met the inclusion criteria. Following variables were associated with a higher risk of M-PM: Right-sided colonic cancer (1-year: right colon vs. rectum, 0.60% (0.22, 0.98) and 3-year: 0.93% (0.34, 1.51)), advanced tumour category (T4- vs. T1-category 1-year: 2.97% (2.19; 3.75) and 3-year: 6.12% (4.98; 7.25)) and lymph node metastasis(N2 vs. N0 1-year: 2.58% (1.87; 3.27) and 3-year: 4.32% (3.29; 5.34)).

A subanalysis revealed that the positive resection margins were associated with an increased risk of M-PM (1-year: R1 vs. R0: 4.16% (1.77, 6.54) and 3-year: 6.18% (2.81, 9.55).

Conclusion

Patients with right-sided colonic cancer, high T-category, lymph node metastasis, and positive resection margins have a higher risk of developing peritoneal metastases. Therefore, a close follow-up program is recommendable.

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C79
INCIDENCE AND PREVALENCE OF PERITONEAL METASTASES AMONG DANISH PATIENTS WITH COLORECTAL CANCER

S. Ravn[1], C.F. Christiansen[2], U. Heide-Jørgensen[2], R.H. Hageman-Madsen[3], V.J. Verwaal[1], L.H. Iversen[1]

[1]Department of Surgery, Colorectal Surgical Unit, Aarhus University Hospital - Aarhus (Denmark), [2]Department of Clinical Epidemiology, Aarhus University Hospital - Aarhus (Denmark), [3]Department of Pathology, Lillebaelt Hospital - Vejle (Denmark)

Objectives

To determine the incidence and prevalence of peritoneal metastases (PM) among Danish colorectal cancer (CRC) patients.

Methods

In a register-based population study, CRC patients were identified between 2006–2015 in the Danish Colorectal Cancer Group database. PM was identified using the Danish National Patient Registry and the Danish National Pathology Registry. Patients were excluded if another cancer occurred within 5 years prior to CRC diagnosis.

Synchronous PM (S-PM) was defined as the presence of a PM diagnosis within ± 180 days from the date of CRC diagnosis.

The cumulative incidence (risk) of metachronous PM (M-PM) was defined as the occurrence of PM after curative CRC surgery and estimated among patients who were free of distant metastases and survived 180 days after CRC diagnosis. Another cancer and death were treated as competing risks.

Results

During 2006–2015, 37,734 patients were included. The prevalence of diagnosed S-PM increased from 2% in 2006 to 5% in 2015.

In total, 22,582 underwent curative CRC surgery. The 1-year risk of M-PM was 0.9% (95% CI:0.8;1.1) increasing to 3.1% (95% CI: 2.8;3.4) after 9 years.

Conclusion

The prevalence of PM seems to have increased over time, which may be due to an increasing awareness and better registration rather than to change in biology.

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C80
PATIENT-REPORTED OUTCOMES SUPPORTING AN INDIVIDUALIZED FOLLOW-UP AFTER CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY. A STUDY PROTOCOL

S. Ravn[1], H.V. Thaysen[1], L. Seibæk[2], L.H. Iversen[1]

[1]Department of Surgery, Colorectal Surgical Unit, Aarhus University Hospital - Aarhus (Denmark), [2]Department of Gynaecology and Obstetrics, Aarhus University Hospital - Aarhus (Denmark)

Objectives

Patient reported outcome (PRO) has gained increasing importance as a method to evaluate postoperative outcomes. PRO is considered a useful instrument to screen for physical, functional and psychosocial problems after treatment, monitor disease progression or therapeutic response, improve communication, and heighten the awareness of patient's health related quality of life (HRQoL). The aim was to develop and evaluate an individualized cancer follow-up increasing patient involvement by focusing on patient's need, activation and HRQoL supported by PRO.

Methods

In a clinical case-control trial from 2017–1019, patients are continuously treated with cytoreductive (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) and followed in the out-patient clinic at 3, 6, 12, 18, 24, 36, 48 and 60 months postoperatively. Both CRS+HIPEC procedures and the follow-up are performed by the same consultant surgeons.

Within the study period, consultations are completed without PRO the first year thereby serving as "controls"; whereas consultations the second year are based on PRO, thus composing the intervention aiming to increase patient involvement. By an electronic system, PRO data are visually presented for the consultant, and with this as the underlying basis the consultation is performed. Outcomes as patient's need, involvement, activation and HRQoL, are assessed shortly after each consultation using The Patient activation measurement (PAM), the European Organization for Research and Treatment of Cancer (EORTC) and Generic questions concerning patient involvement. Measurements of outcome differences are compared between the two groups "controls" and "interventions".

Conclusion

It is expected that the intervention using PRO as the basis of an individual consultation will increase patient involvement by identifying patient's need, accede patient activation and consequently improve HRQoL.

C81
TREATMENT PATHWAYS AND OUTCOME OF PATIENTS WITH COLORECTAL PERITONEAL METASTASIS AT A NATIONAL PERITONEAL TUMOUR CENTRE

S. O'dwyer, A. Larentzakis, O. Aziz, C. Selvasekar, P. Fulford, A. Renehan, M. Wilson

The Christie Colorectal and Peritoneal Oncology Centre - Manchester (United Kingdom)

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Objectives

The introduction of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) as a treatment option for patients with colorectal peritoneal metastases (CRPM) in the United Kingdom National Health Service has been largely centralised to nationally approved peritoneal tumour centres. This study describes the pattern of referrals as well as short- and long-term outcomes achieved for CRPM patients managed through one such centre.

Methods

A prospective register was used to record referrals, demographics, prior treatment pathways, and specialist multidisciplinary team (MDT) decisions for patients with CRPM referred to a UK national peritoneal tumour centre between 2002–2015. Peritoneal cancer index (PCI) was recorded intra-operatively and complete cytoreduction was deemed when a CC0 and CC1 was achieved. Complications were classified using NCI CTAE.v.4. Median overall survival (OS) was estimated using Kaplan-Meier curves. OS was compared between two groups: 1) Patients selected to undergo CRS/HIPEC with or without systemic chemotherapy versus 2) Patients treated with surgery and/or chemotherapy alone.

Results

Over the 13-year study period, 286 patients with CRPM were referred to the centre. Despite a trend towards an annual increase in numbers of referrals, the proportion of patients selected for CRS/HIPEC decreased from 64.5% in 2002–09, to 40% in 2010–12, and 37.1% in 2013–15 ($p < 0.017$). 169 (59.1%) patients were not selected for CRS/HIPEC due to: extent of peritoneal disease (40.5%), active systemic disease (28.6%), progressive disease on chemotherapy (11.3%), poor fitness for surgery (9.5%), and patient choice (4.2%). CRS/HIPEC was undertaken in 117 CRPM patients with a median PCI of 7 (range: 0–31) and CC0/1 achieved in 86.3% (n = 101). The mean length of stay in a critical care unit was 2.91 (±0.55) days, and the mean hospital length of stay was 10.55 (±0.38) days. NCI CTAE grade 3/4 complication rates were 9.4%; 30-day mortality was 0.85%. Median OS following CRS/HIPEC was 46.0 months in Group 1 versus 13.2 months in Group 2. There was no significant difference between groups in gender, age, time to referral, number of prior surgical interventions, and pre-referral chemotherapy treatment.

Conclusion

The evolution of a UK national peritoneal treatment centre over 13 years has been associated with increased referral rates and judicious selection for CRS/HIPEC resulting in low complication rates and high OS compared with traditional non-surgical treatments.

C82

PREDICTING SURVIVAL AFTER CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR APPENDIX ADENOCARCINOMA

O. Aziz, I. Jaradat, B. Chakrabarty, C. Selvasekar, P. Fulford, M. Saunders, A. Renehan, M. Wilson, S. O'dwyer

The Christie Colorectal and Peritoneal Oncology Centre - Manchester (United Kingdom)

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Objectives

Appendix adenocarcinomas are rare tumours with propensity for peritoneal metastasis. Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is an established treatment with curative intent, but to date studies reporting survival have been heterogeneous with regards to their patient groups (including other tumour types), interventions (not all patients receiving intraperitoneal chemotherapy), and follow-up (varying surveillance protocols). This study aims to quantify the impact of this intervention on survival in a homogeneous group of patients with appendix adenocarcinoma receiving standardised treatment and follow-up, and determining the impact of prognostic indicators on survival.

Methods

A retrospective analysis of a prospective database at a national peritoneal tumour centre was undertaken where all patients had their appendix pathology reviewed and management planned by a specialised peritoneal tumour multi-disciplinary team. Data was extracted on prognostic indicators including peritoneal cancer index (PCI), completeness of cytoreduction score (CC), pre-operative tumour markers, and histological features. Overall (OS) and disease event-free survival (DeFS) from date of intervention were evaluated using Kaplan Meier curves and univariate Cox proportional hazards regression analysis.

Results

Between 2005–15, 574 patients had CRS/HIPEC for appendix tumours, of which 65 had appendix adenocarcinomas. Median follow-up was 44.3 months. OS (5-year rate) was 55.5%. PCI < 7 was associated with significantly higher OS compared to ≥7 (83% vs 30%, $p < 0.005$). CC0 resulted in significantly higher OS compared to CC1-3 (70% vs 20.4%, $p < 0.005$). Pre-operative CEA <6 was associated with significantly higher OS compared to ≥6 (63.1% vs 14.1%, $p < 0.005$).

DeFS (5-year rate) was 36.1%. PCI < 7 was associated with a significantly higher DeFS compared to ≥7 (60.4% vs 13.3%, $p < 0.005$). CC0 resulted in a significantly higher DeFS compared to CC1-3 (45.3% vs 15.8%, $p = 0.014$). Pre-operative CEA <6 had a significantly higher DeFS compared to ≥6 (43% vs 11.3%, $p < 0.005$). CA19-9 <38 and CA125 <31 did not significantly affect OS or DeFS.

Conclusion

This study quantifies the impact of cytoreductive surgery with hyperthermic intraperitoneal chemotherapy on OS and DeFS for appendix adenocarcinoma, identifying key prognostic indicators that may guide treatment. It supports the referral of these rare tumours to specialist centres with appropriate expertise for initial management and follow-up.

C83

IMPACT OF COLORECTAL LIVER METASTASES VOLUME ON PATIENTS UNDERGOING SIMULTANEOUS LIVER RESECTION IN CYTOREDUCTIVE SURGERY WITH HEATED INTRAPERITONEAL CHEMOTHERAPY

T. Meares, C. Gauci, M. Bock, O. Fisher, N. Alzahrani, S. Valle, W. Liauw, D. Morris

Liver and Peritonectomy Unit, St George Hospital - Sydney (Australia)

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Objectives

To investigate the impact of the number of liver metastases (LM) and compounded liver metastases volume (LMV) on patients with colorectal cancer (CRC) undergoing simultaneous liver resection (LR) and cytoreductive surgery (CRS) with heated intraperitoneal chemotherapy (HIPEC).

Methods

Patients with CRC and LM were identified from the St George Hospital CRS/HIPEC database. Impact of number of LM as well as LMV on outcomes were assessed. LMV was calculated based on histopathological dimensions. Patients were stratified according to peritoneal cancer index (PCI) (0–5, 6–10, ≥11), number of LM (1, 2–3, ≥4), and LMV tertiles.

Results

60 of 299 (21.9%) patients underwent simultaneous LR and CRS/HIPEC. Median number of LM was 1 (range 1–11). Median compounded LMV was 4189 mm^3. Median cohort survival was 32 months (95% CI 23–68 months) with 3- and 5-year survival of 42.6% and 29.9% respectively. There was no survival difference when stratifying groups according to number of LM or LMV. However, significant survival differences were found when accounting for LM, LMV and PCI. Patients with LM = 1 and a PCI of 0–5 had a median survival of 92 months. Patients with the same number of LM but PCI ≥ 11 had a survival of 17 months ($p = 0.04$). Patients with the same (PCI 0–5) but LM ≥4 had a median survival of 21 months ($p = 0.03$). Patients with moderate volume disease (PCI 6–10) and a single liver lesion had a median survival of 35 months, compared to the same PCI but with ≥4 liver lesions where the median survival was 11 months. When accounting for PCI, there was found to be an equally synergistic impact of liver metastases volume on overall patient survival. That is, as overall volume increased survival decreased. Corrected for age, sex, PCI and number of LM, both PCI ≥11 and LM ≥ 4 were independent negative prognostic factors (HR 6.22, 95% CI 2.04–18.97 and HR 2.95 95% CI 1.02–8.50). No independent effect of LMV was identified.

Conclusion

Simultaneous LR and CRS/HIPEC can achieve good oncological outcomes in colorectal cancer, however, this is limited to patients with PCI ≤10 and LM ≤ 4. This should be considered when evaluating patients for surgery.

C84
AN UPDATE ON THE INCIDENCE, RISK FACTORS, MANAGEMENT AND CLINICAL SEQUALAE OF POSTOPERATIVE PANCREATIC FISTULA FOLLOWING CYTOREDUCTIVE SURGERY AND HIPEC

C. Gauci, T. Meares, O. Fisher, M. Alshahrani, N. Alzahrani, S. Valle, W. Liauw, D. Morris

Liver and Peritonectomy Unit, St George Hospital - Sydney (Australia)

Objectives

To investigate the incidence and consequences of postoperative pancreatic fistula (POPF) in all patients undergoing cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC).

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Methods

Patients were identified from the St George Hospital CRS/HIPEC database. A retrospective analysis was conducted and overall incidence, risk factors, sequalae and management of POPF were studied.

Results

1140 patients had undergone CRS/HIPEC of which 65 (5.7%) developed POPF. Patients with POPF were older (53.5 vs 58.6 years, $p = 0.002$), had a higher peritoneal cancer index (PCI)(median PCI 14 vs 28, $p < 0.001$), longer operation time (median 10.5 vs 8 hours, $p < 0.001$) and required a higher blood transfusion rate intra-operatively (median 8 vs. 3 units, $p < 0.001$). Splenectomy and gastrectomy were significant risk factors for developing POPF ($p < 0.001$ and $p = 0.0018$). Clavien-Dindo grade 3/4 complications and return to theatre occurred more frequently in POPF patients (both $p < 0.001$). POPF patients had significantly higher rates of in-hospital death (7.7 vs 1.5%, $p < 0.001$). POPF led to longer hospital length of stay (LOS) (median 37 vs 20 days, $p < 0.001$). There was no difference in overall long-term survival of patients developing POPF. The median time to diagnosis of POPF was 7 days. 48 patients required radiological drains to be placed. Fistula treating drains were left in place for a median 30.5 days (range 5–96 days). 7 patients were discharged with drains. Other treatment of POPF included total parenteral nutrition (TPN), octreotide, 'nil by mouth', and ERCP with intervention in 7 cases.

Conclusion

There are multiple risk factors for POPF which are non-modifiable. POPF remains detrimental to short-term patient outcomes, although long-term survival does not seem to be impaired in patients who develop POPF.

C85

A MULTI-FACETED EXPERIMENTAL APPROACH UNCOVERS A NOVEL THERAPEUTIC STRATEGY FOR COLORECTAL PERITONEAL CARCINOMATOSIS

C.A.J. Ong, J. Hendrikson, W.H. Ng, X. Qiu, J.W.S. Tan, N.B. Shannon, C.S. Chia, G.H.C. Tan, K.C. Soo, O.L. Kon, M.C.C. Teo

National Cancer Centre Singapore - Singapore (Singapore)

Objectives

1) To investigate the effect on paracrine signalling conferred by ascites in colorectal peritoneal carcinomatosis (CPC) using a combination of *in vitro*, *in silico* and *in vivo* mouse model experiments 2) To demonstrate proof of principle that targeting paracrine signalling provides a novel therapeutic strategy in CPC.

Methods

Ascitic fluid and peritoneal nodules were collected from patients undergoing cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) for colorectal peritoneal carcinomatosis (CPC) (n = 15). 2 cell lines representative of CPC were treated with the ascitic sample to determine the cellular phenotype activated by paracrine signalling. *In silico* bioinformatics analyses were performed to discover pathways upregulated via paracrine signalling after treatment with cell-free ascites. Validation of *in vitro* and *in silico* findings was performed on matched primary colorectal tumours and peritoneal metastasis via immunohistochemistry. Inhibition experiments were performed on a novel model of CPC developed in our laboratory.

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Results

The presence of ascites was found to be an independent prognostic factor in 121 patients who underwent CRS and HIPEC for CPC in our institution. Cell lines treated with ascites increased the proliferation, migration and settling of suspension cells *in vitro* ($p < 0.05$). 0.1% of ascites in cell culture medium was sufficient to maintain cell viability, highlighting the biological potency of ascites. Gene set enrichment analysis of cell lines after treatment with ascites uncovered STAT3 pathway to be highly upregulated, providing a rational therapeutic opportunity targeting paracrine signalling. Immunohistochemistry of matched peritoneal metastasis and primary colorectal cancer from the same patients ($n = 6$) confirmed STAT3 pathway to be highly relevant in CPC. Intra-peritoneal instillation of Napabucasin, a novel STAT3 inhibitor, greatly decreased the modified peritoneal carcinomatosis index in a mouse model of CPC, providing proof of concept of therapeutic efficacy.

Conclusion

We have demonstrated using a series of *in vitro*, *in silico* and *in vivo* experiments to provide proof of concept of an entirely novel therapeutic strategy targeting paracrine signalling in CPC. Clinically, this can be used in the neoadjuvant, intra-operative and adjuvant settings with impactful clinical relevance.

C86
OUTCOME OF CYTOREDUCTIVE SURGERY+HIPEC IN LOW VOLUME COLORECTAL CANCER WITH PERITONEAL METASTASISIS

M. Rahman, N. Alzahrani, S. Valle, W. Liauw, D. Morris

St George Hospital - Sydney (Australia)

Objectives

The purpose of this study was to look at the outcome of Cytoreductive Surgery+HIPEC (Heated Intraperitoneal Chemotherapy) in low volume Colorectal Cancer with peritoneal metastasis.

Methods

A total of 1208 Cytoreductive Surgeries+HIPEC have been performed during 1996–2016 at St George Hospital, Sydney, Australia. This included 359 with Colorectal Cancer and peritoneal metastasis. Of these patients, a total of 94 had low volume (Peritoneal Carcinoma Index less than or equal to 5). 1, 3 and 5 year survival, tumour free periods, hospital and ICU length of stay was extracted from the data. A number of prognostic factors were also anlaysed including but not limited to gender, age, co-morbidities, type of HIPEC, Completeness of cytoreduction(CC) outcomes and total operative hours.

Results

The median survival was 75.6 months. The mean PCI was 3. The disease free survival and overall survival rate at 1,3 and 5 years was 61%, 30%, 25%, 94%, 74% and 58% respectively. The average hospital length of stay was 20.4 days and the median ICU admission was 2.5 days. Morbidity with grade 3 and 4 complications was observed in 22% of the cohort and 0 mortality recorded. Mean operative requirements of 6 hours was observed with a mean pre-CEA of 37.4.

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Conclusion

Cytoreductive Surgery+HIPEC should be considered standard of care for patients with colorectal cancer and low volume peritoneal metastasis.

C87

LONG-TERM SURVIVAL AFTER CYTOREDUCTIVE SURGERY AND HYPERTHERMIC CHEMOTHERAPY IS POSSIBLE FOR PATIENTS WITH COLORECTAL CANCER PERITONEAL METASTASIS

S. Hurton[1], Y. Xu[1], J. Rivard[2], M.L. Quan[1], L. Mack[1], W. Temple[1], A. Bouchard-Fortier[1]

[1]University of Calgary - Calgary (Canada), [2]University of Manitoba - Winnipeg (Canada)

Objectives

Patients with colorectal peritoneal metastases (CPM) have a median survival of 12–18 months when treated with palliative chemotherapy. However, a subset of these patients could benefit from cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC). There is little data on the long-term results of CRS-HIPEC in patients with CPM. The aim of this study was to determine the 5-year actual and actuarial disease-free survival (DFS) and overall survival (OS) of patients undergoing CRS-HIPEC for CPM.

Methods

All consecutive patients with CPM who underwent CRS-HIPEC were identified within the institutional database in Calgary, Canada between 2000–2014. Patients were stratified based upon survival ≥5 years and <5 years. Kaplan-Meier curves were used to estimate 5-year OS and DFS. Univariate analysis was performed to determine factors associated with 5-year OS.

Results

There were 83 patients identified with CPM who underwent CRS-HIPEC between 2000–2014 at a single institution with a median follow-up of 29.9 months. For this cohort, intraoperative median PCI was 13 (IQR: 5–21), and complete cytoreduction (CCR0) was possible in 82 patients (97.6%). There was a trend toward patients with lower comorbidity score surviving >5 years (score of 0 in 50.0% vs 30.1%, $p = 0.41$). The majority of patients received perioperative systemic chemotherapy. At 5 years, there were a total of 16 patients still alive, for a 5-year actual OS of 19.2%. There were 12 patients free of disease at five years, for a 5-year actual DFS for our cohort of 14.5%. This includes three patients who had PCI >20 (PCI = 21, 22, 39). On univariate analysis, factors associated with long-term survival were operative duration >6 hours ($OR = 0.11$, $p < 0.01$) and lower PCI ($OR = 0.92$, $p = 0.02$). Choice of HIPEC agent, histology, nodal status, grade of tumor, age, gender, and year of OR were not significant in univariate analysis.

Conclusion

In patients who underwent CRS-HIPEC for CRC, the 5-year actual OS was 19.5%, and 14.5% of patients were free of disease at 5 years. With these results, CRS-HIPEC combined with systemic chemotherapy should be standard of care for those with CPM to obtain the optimal long-term disease-free and overall survival. As we had 3 patients with PCI > 20 achieved long term survival, there may be a role for CRS-HIPEC in ideal candidates with high PCI.

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C88
MENTORED SET-UP OF A PERITONEAL MALIGNANCY CENTRE: EARLY OUTCOMES IN 50 PATIENTS

N. Ansari[1], K.G.M. Brown[1], C.E. Koh[1], K. Mcbride[2], D. Steffens[3], J.M. Young[4], C.J. Young[5], M.J. Solomon[6], B.J. Moran[7]

[1]Royal Prince Alfred Hospital, Surgical Outcomes Research Centre (SOuRCe) - Sydney (Australia), [2]RPA Institute of Academic Surgery - Sydney (Australia), [3]Surgical Outcomes Research Centre (SOuRCe) - Sydney (Australia), [4]Surgical Outcomes Research Centre (SOuRCe), RPA Institute of Academic Surgery - Sydney (Australia), [5]Royal Prince Alfred Hospital, RPA Institute of Academic Surgery - Sydney (Australia), [6]Royal Prince Alfred Hospital, RPA Institute of Academic Surgery, Surgical Outcomes Research Centre (SOuRCe) - Sydney (Australia), [7]Peritoneal Malignancy Unit, North Hampshire Hospital - Basingstoke (United Kingdom)

Objectives

Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) is an accepted therapeutic approach in selected patients with peritoneal malignancy. This study describes early outcomes in the index 50 patients managed with CRS and HIPEC in a newly established peritoneal malignancy centre in Sydney, Australia under the guidance of an experienced peritoneal malignancy mentor from the Peritoneal Malignancy Institute, Basingstoke, UK.

Methods

This is a retrospective analysis of a prospective database of early outcomes in the first 50 patients who underwent CRS and HIPEC between April 2017 and April 2018 at a newly established peritoneal malignancy centre in Sydney, Australia.

Results

A total of 136 patients were referred and reviewed at the multidisciplinary team meeting with 50 (26 male) patients undergoing CRS and HIPEC. Of these, 47/50 (94%) patients underwent complete cytoreduction while 3 (6%) patients had maximal tumour debulking surgery. All patients who had a complete cytoreduction received HIPEC. Tumour pathology was of appendix origin in 22/50 (44%) and colorectal peritoneal metastases in 22/50 (44%). Median length of surgery was 7.5 hours (IQR = 5.8 to 10). Median length of stay was 13.5 days (IQR = 10.3 to 21.5). There was no 30-day mortality and 12.5% major morbidity defined as Clavien-Dindo grade III/IV.

Conclusion

This study demonstrates that it is safe and feasible to establish a peritoneal malignancy centre under the guidance of an experienced peritoneal malignancy surgeon and mentor. These reported early outcomes are encouraging and comparable to other international centres.

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C89
QUALITY OF LIFE FOLLOWING CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY: SHORT TERM OUTCOMES FROM A PROSPECTIVE COHORT STUDY

N. Ansari[1], C.E. Koh[1], K.G.M. Brown[1], D. Steffens[2], J.M. Young[3], C.J. Young[3], M.J. Solomon[4], B.J. Moran[5]

[1]Royal Prince Alfred Hospital, Surgical Outcomes Research Centre (SOuRCe) - Sydney (Australia), [2]Surgical Outcomes Research Centre (SOuRCe) - Sydney (Australia), [3]Surgical Outcomes Research Centre (SOuRCe), Institute of Academic Surgery - Sydney (Australia), [4]Royal Prince Alfred Hospital, Surgical Outcomes Research Centre (SOuRCe), Institute of Academic Surgery - Sydney (Australia), [5]Peritoneal Malignancy Institute, North Hampshire Hospital - Basingstoke (United Kingdom)

Objectives

Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) has been demonstrated to be an effective treatment option for selected patients with peritoneal surface malignancies. The aim of this study is to describe the short-term quality of life (QoL) outcomes following CRS and HIPEC at a newly established peritoneal malignancy centre.

Methods

Consecutive patients undergoing CRS and HIPEC at the Royal Prince Alfred Hospital, Sydney, Australia between April 2017 and April 2018 were recruited. QoL was measured using the short-form 36 (SF-36 version 2) questionnaire and expressed as physical (PCS) and mental component score (MCS), with higher scores representing better QoL. Data was collected at baseline, pre-discharge, 3 months and 6 months postoperative. Trajectories of the PCS and MCS were described.

Results

Among 50 patients that underwent CRS and HIPEC, 46 (92%) entered the study. Most presented with colorectal (44%) and appendiceal origin (44%) peritoneal metastases. Median [IQR] baseline PCS (43.1 [35.3 to 55.8]) and MCS (50.5 [43.7 to 55.7]) decreased at pre-discharge (PCS = 34.25 [28.1 to 41.0] and MCS = 48.6 [37.8 to 55.5]); returning to baseline within 3 months (PCS = 43.0 [37.6 to 51.3] and MCS = 52.5 [45.4 to 58.2]). The PCS remained unchanged at 6 months (40.3 [37.9 to 51.1]) whereas MCS had a slightly increase (52.3 [41.0 to 57.0]).

Conclusion

QoL returned to baseline within 3 months postoperative and remained relatively stable thereafter. In the short-term, CRS and HIPEC can be performed with acceptable QoL outcomes. Further studies are needed to describe the long-term QoL trajectories.

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C90
PRE-OPERATIVE NEUTROPHIL-LYMPHOCYTE RATIO PREDICTS FOR POST-OPERATIVE INFECTIVE COMPLICATIONS IN PATIENTS UNDERGOING CRS AND HIPEC

W. Wang, C.J.J. Seo, G.H.C. Tan, C.S. Chia, J.C.A. Ong, K.C. Soo, M.C.C. Teo

National Cancer Centre Singapore - Singapore (Singapore)

Objectives

Post-operative infectious complications have been associated with poor survival outcomes. In this study, we aim to investigate factors that may predict development of post-operative infectious complications in patients undergoing cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC).

Methods

Patients who have undergone CRS/HIPEC in our institution between January 2001 and December 2016 were included. A review of prospectively collected demographic and clinico-pathological data was performed. Pre-operative biomarkers such as serum albumin, neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR), were collected if they were taken within 1 week before CRS and HIPEC. Univariate and multivariate logistic regression were performed.

Results

248 patients were included in the study. The median age of our patients was 54 years (range: 14 to 76). The most common primary site of tumour was ovarian cancer (34.7%, n = 86), followed by colorectal (21%, n = 77) and appendiceal (22.6%, n = 56) cancers. On multivariate analysis, an elevated NLR > 2.7 ($p = 0.04$; HR = 2.829, 95% CI 1.40–5.71), visceral resection ($p = 0.43$; HR = 3.359, 95% CI 1.04–10.89) and higher PCI score ($p = 0.001$, HR:1.062, 95% CI 1.02–1.10) were independently associated with development of infectious complications. Age, performance status, history of diabetes, site of primary tumour and serum albumin were not found to be significant.

Conclusion

Our results show that elevated NLR was independently prognostic for post-operative infectious complications, suggesting that there might be a link between preoperative systemic inflammation, post-operative complications and survival outcomes. Some authors have suggested that a surge in neutrophils in the operative bed can lead to tumour progression. Although more work needs to be done to elucidate the exact mechanism, clinicians may consider the use of NLR as a simple biomarker to identify patients at risk of post-operative infectious complications.

C91
EVALUATION OF MORBIDITY, MORTALITY AND HEALTH RELATED QUALITY OF LIFE FOR CONCENTRATION-BASED AND BSA-BASED HIPEC IN COLORECTAL PERITONEAL SURFACE MALIGNANCY TREATMENT

L. Lemoine[1], E. Thijssen[2], R. Carleer[2], P. Sugarbaker[3], K. Van Der Speeten[1]

[1]Dpt of Medicine and Life Sciences, Hasselt University; Dpt of Surg. Oncol., Ziekenhuis Oost-Limburg - Hasselt, Genk (Belgium), [2]Dpt of Sciences, Applied and Anal. Chem., Hasselt University - Hasselt (Belgium), [3]MedStar Washington Hospital Center - Washington DC (United States)

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Objectives

At present, the combination therapy of CRS and HIPEC is considered standard of care for colorectal peritoneal surface malignancy (PSM) treatment. Concentration-based and BSA-based are the two standards HIPEC dosing regimens used in current clinical practice. However, little is known about the potential difference in morbidity and mortality between the two regimens and their effect on patients' health related quality of life (HRQOL).

Methods

The dosing regimens were clinically and pharmacologically evaluated in a randomized clinical trial, the COBOX trial (NCT03028155). Patients diagnosed with colorectal PSM were randomized to either concentration-based or BSA-based HIPEC. Oxaliplatin was administered at a dose of 460 mg/m² (BSA-based) or 460 mg/m^2in 2 L/m20.9% NaCl carrier solution (concentration-based) during a 30-minute HIPEC. Three-month overall morbidity and mortality were evaluated using the Clavien-Dindo grading system. HRQOL was assessed by means of the validated EORTC QLQ-C30 and SF-36 questionnaires.

Results

At present, 29 patients were randomized to concentration-based HIPEC (n = 14) and BSA-based HIPEC (n = 15). Although there was a significantly higher toxicity, denoted as a higher area-under-the-curve of the plasma compartment, in the concentration-based group (p = 0.005), there was no significant difference in three-month minor and major morbidity between both groups. One in-hospital death was reported in the BSA-based group. At discharge, patients treated with concentration-based HIPEC had a lower HRQOL (p = 0.044). Three months postoperative, patients in the concentration-based group had a lower functional score (p = 0.034).

Conclusion

Although there is no difference in three-month overall morbidity and mortality between patients treated with either concentration-based or BSA-based HIPEC, HRQOL is lower in the concentration-based group.

C92

TREATMENT OF PERITONEAL DISSEMINATION IN STOMACH CANCER PATIENTS WITH CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC): FIRST RESULTS OF THE PERISCOPE I STUDY

R.T. Van Der Kaaij[1], E.C.E. Wassenaar[2], W.J. Koemans[1], K. Sikorska[3], H. Boot[4], C. Grootscholten[5], J.H.M. Schellens[6], M. Los[7], K.J. Hartemink[1], A.A.F.A. Veenhof[1], C.P. Hahn[8], A.P.I. Houwink[8], D. Boerma[2], B. Van Ramshorst[2], J.W. Van Sandick[1]

[1]Department of Surgical Oncology – The Netherlands Cancer Institute - Amsterdam (Netherlands), [2]Department of Surgery – St. Antonius Hospital - Nieuwegein (Netherlands), [3]Department of Biometrics – The Netherlands Cancer Institute - Amsterdam (Netherlands), [4]Department of Gastroenterology – The Netherlands Cancer Institute - Amsterdam (Netherlands), [5]Department of Medical Oncology – The Netherlands Cancer Institute - Amsterdam (Netherlands), [6]Department of Clinical Pharmacology – The Netherlands Cancer Institute - Amsterdam (Netherlands), [7]Department of Medical Oncology – St. Antonius Hospital - Nieuwegein (Netherlands), [8]Department of Anaethesiology – The Netherlands Cancer Institute - Amsterdam (Netherlands)

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Objectives

Hyperthermic intraperitoneal chemotherapy (HIPEC) has been shown effective for peritoneal seeding from various cancer types. Its role in gastric cancer is as yet undetermined. This dose-finding phase II study was designed to assess the maximum tolerated dose (MTD) of intraperitoneal docetaxel in combination with a fixed dose of intraperitoneal oxaliplatin in gastric cancer patients with limited peritoneal dissemination, and to assess its safety and feasibility when used in combination with gastrectomy and cytoreductive surgery, after systemic chemotherapy.

Methods

Patients with advanced gastric adenocarcinoma (cT3–cT4) with limited peritoneal metastases and/or tumour positive peritoneal cytology were included. An open HIPEC technique was used with 460mg/m^2 hyperthermic oxaliplatin (30 minutes) followed by normothermic docetaxel (90 minutes) in escalating dosages (0, 50, 75 mg/m^2). Primary endpoint was treatment related toxicity.

Results

Between 2014 and 2017, 37 patients were included. Twelve patients did not undergo the full study protocol because of disease progression during systemic chemotherapy, toxicity of systemic chemotherapy, irresectability of the primary tumour or because of gross peritoneal tumour dissemination at laparotomy. The remaining 25 patients completed the full study protocol. Of them, 4 patients were treated in dose level 1 (0 mg/m^2 docetaxel), 6 patients in dose level 2 (50 mg/m^2), and 4 patients in dose level 3 (75 mg/m^2). In this latter dose level, two dose-limiting toxicities (DLTs) occurred, both associated with a postoperative ileus: one aspiration leading to resuscitation (unsuccessful), and one caecal perforation necessitating acute surgery. Thereafter, another 11 patients were treated at dose level 2, and no more DLTs occurred. Overall, serious adverse events occurred in 17 of 25 patients. The re-operation rate was 16% (n = 4), and treatment related mortality was 8% (n = 2; both in dose level 3).

Conclusion

In gastric cancer patients with limited peritoneal dissemination, gastrectomy combined with cytoreduction and HIPEC was feasible using 460 mg/m^2 oxaliplatin and 50 mg/m^2 docetaxel. The efficacy of this treatment in improving prognosis must be explored in future studies.

C93

SURVIVAL AND COST-EFFECTIVENESS OF HIPEC IN COLORECTAL PERITONEAL CARCINOMATOSIS TREATED AT IPO PORTO

A. Sousa[1], M. Peyroteo[1], J.C. Pereira[1], P. Redondo[2], F. Senra[1], D. Brito[1], F. Sousa[1], M. Fernandes[1], J.F. Videira[1], J. Abreu De Sousa[1]

[1]Surgical Oncology IPO Porto - Porto (Portugal), [2]Ouctome Research Lab - Porto (Portugal)

Objectives

Treatment of colorectal (CCR) metastasis has evolved radically and long-term survival for resectable oligometastatic disease is possible. Cytoreduction surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) is being increasingly used in selected patients with peritoneal carcinomatosis (pc) as part of the multidisciplinary strategy contributing to a survival at five years between 25–40%. We've

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performed a survival and costs analysis associated with CRS/HIPEC for patients with pcCCR/appendicular cancer (AC) and established the level of cost effectiveness associated with this complex procedure at our center.

Methods

From our database of 351 patients we selected the patients treated between January 2010 and December 2017. We determined the overall survival (OS) for patients with pcCCR and pcAC who underwent CRS/HIPEC. Furthermore, we performed an incremental-cost effectiveness ratio analysis at 12 months after treatment comparing patients who underwent HIPEC/CRS between 2014 and 2015 and the patients assigned to systemic chemotherapy.

Results

A total of 187 patients were treated and 206 procedures were performed. OS for the entire group was 63.4% at 3 years and 53% at 5 years. When analyzed separately, 91 patients had pcCCR carcinomatosis and 96 had pcAC (accounting for 99 and 107 procedures respectively). OS was 51.4% and 34.1% at 3 and 5 years for CCR. OS for AC was 85.1% and 75.5% at 3 and 5 years.

The cost per patient for CRS/HIPEC from pcCCR/pcAC was 7,949.68 € for the first year after treatment and 11,916.95€ for the systemic chemotherapy group. We determined a survival gain of one month after the first year for the CRS and HIPEC group when compared with standard treatment. A saving of 3,967.27€ with an increased survival of one month by the first year was obtained for the HIPEC population.

Conclusion

Although commonly analyzed together and treated with the same CRS/HIPEC technique, pcCCR and pcAC have different prognostic implications. Despite the evolution of systemic therapy, this form of CCR metastasis has suboptimal results when compared with liver disease suggesting a different in biologic behavior.

At our center, treatment of pcCCR with CRS and HIPEC is more cost-effective than standard palliative chemotherapy. Careful patient selection, the retrospective nature of the study as well as differences regarding health care funding could account for such results.

C94
WIDE VARIATION IN INTRAPERITONEAL CHEMOTHERAPY CONCENTRATIONS DURING HIPEC IN PATIENTS TREATED FOR COLORECTAL PERITONEAL METASTASES

F.M.K. Elekonawo[1], W.J. Van Eden[2], W.Y. Van Der Plas[3], R.S.G. Ewalds[1], A.J.A. Bremers[1], P.H.J. Hemmer[3], N.F.M. Kok[2], S. Kruijff[3], A.G.J. Aalbers[2], P.R. De Reuver[1]

[1]Radboud University Medical Center - Nijmegen (Netherlands), [2]The Netherlands Cancer Institute - Amsterdam (Netherlands), [3]University Medical Center Groningen - Groningen (Netherlands)

Objectives

Selected patients with colorectal peritoneal metastases (PM) are treated with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). In clinical practice, the concentration of intraperitoneal chemotherapy is a result of several factors i.e. the administered dose (based on body surface area) and perfusate volume (determined by intraperitoneal volume). The aim of this study was to gain insight into the final intraperitoneal chemotherapy concentration during the HIPEC-procedure and its potential effects on outcome.

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Methods

This was a retrospective, multicenter study. Consecutive patients with colorectal PM who were treated with CRS-HIPEC between 2010 and 2017 in three tertiary referral centers were included. Patient data were retrieved from prospectively developed databases. Type of intraperitoneal chemotherapy, chemotherapy dose and total circulating volume of the carrier solution were used to calculate the final chemotherapy concentration in milligram (mg) per liter (L). Assessed outcomes were intraoperative chemotherapy concentration, postoperative complications and disease free and overall survival. Univariable and multivariable logistic regression, cox regression and survival analyses were performed.

Results

Three hundred and twenty patients were included of whom 220 patients received intraperitoneal Mitomycin C (MMC) and 100 patients oxaliplatin (OXA). Median total MMC concentration was 13.3 mg/L (range 7.0–76.0). Median final OXA concentration was 156.0 mg/L (range 91.9–377.6). Median circulating volume in all patients was 5.0 L (range 0.7–10.0). Grade ≥3 complication rate was 23.4% (n = 75). Median overall survival was 36.9 months (IQR 19.5–62.9). Chemotherapy concentration of MMC or OXA were neither associated with postoperative complications nor survival outcomes.

Conclusion

CRS-HIPEC is performed with a wide variation in intraperitoneal chemotherapy concentrations. Concentration did not significantly influence postoperative complications or survival.

C95

POSTOPERATIVE COMPLICATIONS AFTER HIPEC WITH OXALIPLATIN AND DOCETAXEL IN GASTRIC CANCER PATIENTS WITH PERITONEAL DISSEMINATION

W.J. Koemans[1], R.T. Van Der Kaaij[1], E.C.E. Wassenaar[2], K. Sikorska[3], H. Boot[4], C. Grootscholten[4], M. Los[5], K.J. Hartemink[1], A.A.F.A. Veenhof[1], C.P. Hahn[6], A.P.I. Houwink[6], D. Boerma[7], B. Ramshorst[7], J.W. Sandick[1]

[1]Department of Surgical Oncology - The Netherlands Cancer Institute - Amsterdam (Netherlands), [2]Department of Surgery - St. Antonius Hospital - Nieuwengein (Netherlands), [3]Deparment of Biometrics - The Netherlands Cancer Institute - Amsterdam (Netherlands), [4]Department of Gastrointestinal Oncology - The Netherlands Cancer Institute - Amsterdam (Netherlands), [5]Department of Medical Oncology - St. Antonius Hospital - Nieuwegein (Netherlands), [6]Department of Anaesthesiology - The Netherlands Cancer Institute - Amsterdam (Netherlands), [7]Department of Surgery - St. Antonius Hospital - Nieuwegein (Netherlands)

Objectives

In Asian countries, Hyperthermic Intraperitoneal Chemotherapy (HIPEC) is widely used in gastric cancer patients with peritoneal dissemination. This is not the case in Europe. Its efficacy remains to be established, and more data are needed on the associated postoperative complication risk. A prospective dose escalation trial (PERISCOPE I) was conducted to assess the feasibility of HIPEC with oxaliplatin and docetaxel in gastric cancer patients with synchronous peritoneal carcinomatosis. Postoperative complications were systematically recorded.

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Methods

In two experienced HIPEC centres, patients with limited peritoneal dissemination of a locally advanced, resectable gastric adenocarcinoma were treated with (sub)total gastrectomy, cytoreductive surgery and HIPEC provided that preoperative systemic chemotherapy was without disease progression. Intraoperative intraperitoneal chemotherapy consisted of oxaliplatin (460 mg/m^2) for 30 minutes at 41–42°C, followed by docetaxel in escalating dosages (0, 50, 75 mg/m^2) for 90 minutes at 37°C. Complications were scored using Common Toxicity Criteria version 4.03.

Results

In total, 25 patients underwent the full study procedure. Re-admission rate at the intensive care unit was 32% (n = 8). Two patients (8%) died due to a complicated postoperative course: one patient after reanimation following aspiration; another patient from the sequelae of a duodenal stump leakage. Four patients (16%) needed one or more re-operations, firstly because of small bowel ischaemia (n = 2), duodenal stump leakage (n = 1), or colonic perforation (n = 1). Nonsurgical re-interventions involved coil embolization of a mesenteric artery bleeding (n = 1), percutaneous abdominal drainage (n = 5), percutaneous thoracic drainage (n = 3), and endoscopic stent placement for an anastomotic leakage (n = 2). Other serious adverse events were infectious, gastro-intestinal, neurologic, thromboembolic, and haematologic complications. Median postoperative hospital stay was 24 (IQR: 13–32) days.

Conclusion

In the PERISCOPE I study, including gastric cancer patients with synchronous peritoneal carcinomatosis, postoperative complications after HIPEC with oxaliplatin and docetaxel were common and diverse. Postoperative management required a broad multidisciplinary team of various medical and interventional specialists.

C96

A NOMOGRAM FOR PREDICTING PERITONEAL METASTASES IN STAGE II-III COLON CANCER PATIENTS AFTER RADICAL RESECTION

G. Cai, W. Dai, S. Mo, W. Xiang, R. Wang, Q. Li, S. Cai, Y. Xu

Fudan University Shanghai Cancer Center - Shanghai (China)

Objectives

The prediction of metachronous peritoneal metastases (mPM) of colon cancer was poorly studied. In this study, we sought to establish a nomogram model to predict the peritoneal metastases in colon cancer patients.

Methods

Patients with stage II–III colon cancer (adenocarcinoma/mucinous adenocarcinoma/signet ring cell cancer) undergoing radical resection at the Fudan University Shanghai Cancer Center (FUSCC) between 2008 and 2013 were retrospectively analyzed in this study. Cox regression model analysis was performed to assess the prognostic factors for mPM. Nomograms were established to predict mPM free survival, and Harrell's concordance index (c-index) was adopted to evaluate prediction accuracy.

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Results

A total of 509 eligible stage II–III colon cancer patients with long-term follow-up information (more than 36 months) were identified, of whom 39 patients (7.6%) presented with mPM. The median follow-up time was 51 months. Multivariate COX regression analysis suggested that female (HR 6.17, 95%CI 2.65–14.37, P < 0.001), youth (HR 4.97, 95%CI 1.53–16.14, P = 0.008), mucinous histological type (HR 3.12, 95%CI 1.17–8.27, P = 0.023), right-side tumor (HR 3.58, 95%CI 1.65–7.77, P < 0.001), tumor deposit (HR 3.32, 95%CI 1.63–6.74, P < 0.001), less lymph node harvested (LNH) (12 LNHs as cut off point) (HR 3.19, 95%CI 1.39–7.29, P = 0.006) and more than 3 positive lymph nodes (HR 3.48, 95%CI 1.33–9.07, P = 0.006) were significantly correlated with mPM free survival. A nomogram was established and showed considerable predicting accuracy (c-index 0.893, 95%CI 0.812–0.974) in this cohort. Further calibration analysis for nomogram revealed no deviations from the reference line and no need of recalibration.

Conclusion

The nomogram integrating clinicopathological parameters developed in this study can be helpful to identify colon cancer patients who are at high risk of mPM.

C97

NEPHROTOXIC EFFECTS OF CISPLATIN COMBINED WITH MITOMYCIN C IN LAPAROSCOPIC HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY

K. Robinson, R. Kapoor, P. Owusu-Agyemang, J. Cata, P. Mansfield, B. Badgwell

MD Anderson Cancer Center - Houston (United States)

Objectives

Laparoscopic hyperthermic intraperitoneal chemotherapy (HIPEC) has been used to treat various peritoneal malignancies. Cisplatin and mitomycin C are commonly used single chemotherapeutic agents in these procedures and have individually been associated with potential acute kidney injury. There is limited literature on the complications associated with the use of *both* agents, in combination, in HIPEC.

Methods

We retrospectively evaluated patients undergoing laparoscopic HIPEC for gastroesophageal adenocarcinoma using both cisplatin (200 mg) and mitomycin C (30 mg) from September 2016 to October 2017 at MD Anderson Cancer Center. Sodium thiosulfate was given for renal protection. Patient demographics, co-morbidities, chemotherapeutic regimens, perioperative laboratory values, and anesthetic management details were collected.

Results

Twenty-three patients underwent 31 laparoscopic HIPEC procedures. Fifteen (65%) were male, and the median age was 57 years (range 22–77 years). All patients developed a decrease in hemoglobin level, with a median decrease of 1.7 g/dL (range 0.6–2.8 g/dL). Eighteen procedures were associated with an improvement (decrease) in creatinine level. For procedures with an elevation in creatinine, the median increase was 0.06 mg/dL (range 0.03–0.22), with a median decrease in the glomerular filtration rate of 9 mL/min/1.37 m^2 (range 4 to 38). Relevant to postoperative electrolyte management, an 84% incidence of postoperative hypophosphatemia (26/31) and 94% incidence of postoperative hypocalcemia (29/31) were observed. However, not a single case demonstrated acute kidney injury, defined as a 50% increase in creatinine levels above baseline.

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Conclusion

The laparoscopic approach to HIPEC using both cisplatin and mitomycin C in our patient cohort was not associated with an increased incidence of acute kidney injury. A multitude of surgical and anesthetic factors likely contributed to this lack of association. The observed incidence with which our patients encountered hypophosphatemia and hypocalcemia is an important finding for anticipating electrolyte replacement, but further studies are needed to evaluate the exact etiology of these effects in this setting.

C98
REPEATED CYTOREDUCTIVE SURGERY WITH HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY

A. Nissan, S. Goren, A. Ben-Yaacov, D. Perelson, E. Shmueli, D. Aderkad, G. Schtrechman, T. Kaplon, D. Zippel, A. Al-Kurd

Tel Aviv UNI - Ramat Gan (Israel)

Objectives

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) were shown to improve survival in patients with peritoneal surface malignancies. There is limited experience with repeated CRS+HIPEC in patients with recurrent disease. Our Aim is to analyze our cohort of patients with recurrent disease who underwent repeated CRS+HIPEC.

Methods

Prospectively collected database of patients undergoing CRS/HIPEC was reviewed. Patients who underwent more than one CRS/HIPEC were identified. Patient's demographics, short term (peri-operative) and long-term (survival) outcomes were compared between the study group (n = 28) and patients who underwent a single CRS/HIPEC (n = 248). Clavien Dindo (CD) 5-tiered score was used. To predict risk for complications or incomplete cytoreduction, logistic regression was conducted using age, gender, OR time, operative PCI and ASA score. To examine difference in overall (OS) and Disease Free Survival (DFS), between groups, survival analyses were conducted using Kaplan-Meire analyses.

Results

No significant differences were found in terms of demographic, primary diagnosis, intra-operative parameters including EBL, PCI, OR time and CC score as well as in post-operative parameters including ICU stay, hospital stay and complications (including 90 days mortality). Reoperation rate was not statistically different but still noticeable - two times folded among patients with second HIPEC (20% vs. 9.7% respectively, p = .163). Short OR time and low PCI score were correlated with CC-0-1 using logistic regression (OR = 0.805, 95% CI 0.658–0.986, p = .036), (PCI = 0.873, 95% CI 0.826–0.922, p < .001). OR time also showed positive correlation with CD score (OR = 1.172, 95% CI 1.009–1.361, p = .038). There was no difference in overall survival (p = 0.308). However, DFS was lower in the repeated HIPEC group (p = 0.036).

Conclusion

Our results show that CRS+HIPEC can be performed safely in this group of complex patients with good oncological outcome, encouraging us to recommend 2nd or even 3rd CRS+HIPEC procedure to selected patients.

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C99
LAPAROSCOPIC CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY IN PATIENTS WITH COLORECTAL CANCER PERITONEAL METASTASIS

S.C. Chang

Colorectal Surgeon, Division of Surgery, Chhinamedical University Hospital - Taichung

Objectives

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) are widely used in treatment of colorectal cancer peritoneal metastasis (CRC-PM). Traditional open laparotomy has been associated with high surgical complications and prolonged recovery duration.

Methods

We enrolled colorectal cancer patients with peritoneal metastasis which peritoneal cancer index less than 15 on the computed tomographic scan from November 2016 to April 2018 in our institute. Exclusion criteria was unresectable intraabdominal metastasis and extraabdominal metastasis and age more than 70. These patients underwent laparoscopic CRS and HIPEC. We aimed to assess the feasibility, safety, and outcome of this procedure. Surgical morbidity were reported according to the Clavien Dindo Classification.

Results

During this period, 18 patients were enrolled but extensive carcinomatosis was found in 2 patients at the time of laparoscopy who referred to systemic chemotherapy. Median PCI was 4.5 (1–15). Malignant tumor came from appendix (3), right side colon (5) and left side colon (8). Sixteen patients had a complete cytoreduction and HIPEC, 14 (87.5%) laparoscopically, and 2 (12.5%) were converted to open procedure. Intraoperative complication occurred in 4 patients, including diaphragm perforation (2), Massive diaphragmatic hemorrhage (1) and urinary bladder perforation(1). There was one grade 2 morbidity (6.25%) for upper gastrointestinal bleeding and none had major morbidity needing a reoperation. Median length of hospital stay was 9 days (5–15 days) for those completed laparoscopically, 10 days for those converted to an open procedure.

Conclusion

This study demonstrates laparoscopic CS+HIPEC was feasible and safe in selected patients with PCI less than 15 and no small bowel involvement. Longer follow-up and additional studies are required for further analyses.

C100
FIRST EXPERIENCE IN CYTOREDUCTIVE SURGERY AND HIPEC FOR METASTATIC PERITONEAL DISEASE AT RAMON Y CAJAL HOSPITAL: 25 FIRST PATIENTS

L.D. Juez[1], P. Muñoz[1], M. Cuadrado[1], V. Pachón[2], J. Cabañas[1], J. Galindo[1]

[1]Department of General Surgery - Madrid (Spain), [2]Department of Oncology - Madrid (Spain)

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Objectives

Radical cytoreductive surgery (CRS) with intraperitoneal hyperthermic chemotherapy (HIPEC) is considered the current standard treatment for metastatic peritoneal disease in several tumors.

Methods

Between JULY 2015- OCTOBER 2017, 25 radical cytoreduction procedures were performed with administration of hyperthermic intraoperative chemotherapy.

Results

We included 25 patients with peritoneal carcinomatosis (54% males, median age 57.7 years, range 44–77 years). The most frequent origin of carcinomatosis peritoneal was colorectal cancer (54%). Median PC index was 8 (range 0–35). Complication rate (any grade) was 76%, however, severe morbidity rate (Clavien-Dindo III-V) was 36%. CC0-1 was obtained in 100% of patients. We only had 1 surgical reintervention and 0% perioperative mortality. At median follow-up of 10.2 (range 1–22) months, OS was 12.52 months. Median time until recurrence was 9.68 months.

Conclusion

The CRS and HIPEC procedures have a survival benefit in patients with a morbi-mortality comparable to high-volume centers. Our OS and DFS are similar to those described in the literature. The evaluation and selection of patients should be performed by a multidisciplinary team including surgical oncologists, medical oncologists, radiologists and pathologists.

C101

COMPARISON OF LONG TERMS OUTCOMES AFTER SURGICAL MANAGEMENT OF PERITONEAL AND/OR LIVER METASTASIS FROM NEUROENDOCRINE TUMORS

L. Benhaim, M. Faron, M. Gelli, I. Sourrouille, J.Y. Scoazec, A. Berdeloux, J. Hadoux, S. Hescot, C. Patriarche, E. Baudin, D. Goere

Gustave Roussy - Villejuif (France)

Objectives

The peritoneum is a common location for tumor dissemination in patients with low grade neuroendocrine tumors (NET) especially in the case of ileal origin. Peritoneal metastasis (PM) are often associated with other sites and related with shorter survival. Indirect comparisons have suggested that a complete cytoreductive surgery (CRS) could prolong survival in selected patients when compared with incomplete surgery or palliative treatment alone. Yet the exact benefit of this surgical management is unknown. The present study compared the outcomes of patients operated for PM and/or liver metastasis (LM).

Methods

Baseline, surgery characteristics and outcomes of patients who underwent CRS for NET (grade 1 or 2) between 1995 and 2016 in a single institution were retrospectively reviewed using a prospective database. All patients were operated with complete resection of the macroscopic disease (R0 or R1). Tree groups were compared: group LM only, group PM only, group LV+PM. In all three groups the primary tumor was resected during the same surgery or had been removed previously

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Results

Results: Forty patients with LM only were compared to 12 with PM only and 34 with combined LM+PM. There was no difference between groups in regards to the tumor origin, the presence of pre-operative symptoms, the pre-operative treatment, the presence of synchronous lymph nodes, the tumor grade and the number of previous surgeries for NET. Five-year overall survival reached 78% in the LM group, 80% in the PM group and 72% in the LM+PM group ($p < 0.71$). Five-year disease-free survival was 19%, 12% and 17% in the LM, PM and LM+PM groups respectively ($p < 0.45$).

Conclusion

Conclusion: After CRS, the survival of patients with PM was similar to the survival of patients operated for LM alone. The combined resection of LM and PM offers comparable benefits in this selected population. This conclusion needs to be confirmed in larger surgical series but surgery remains a valid therapeutic option in selected cases of PM with or without LM from NET.

C102

HIPEC: CLOSED TECHNIQUE WITH CO2 RECIRCULATOIN IN THE MULTIMODAL TREATMENT OF PERITONEAL CARCINOMATOSIS

E. Ovejero[1], A. Gutiérrez[2], R. Gómez[1], A. López[1], I. Lasa[1], R. Marcos[1], R. Medina[3], L. Jiménez[3], R. Alvarado[3]

[1]FEA Cirugía Hospital Universitario Príncipe de Asturias - Alcalá De Henares. Madrid (Spain), [2]Jefe Clínico Cirugía Hospital Universitario Príncipe de Asturias - Alcalá De Henares. Madrid (Spain), [3]MIR Cirugía Hospital Universitario Príncipe de Asturias - Alcalá De Henares. Madrid (Spain)

Objectives

The capacity to achieve a COMPLETE CYTOREDUCTION during surgery and PCI (Peritoneal Carcinomatosis Index) are the two main PROGNOSTIC FACTORS; to date, we do not really know the true impact of HIPEC (Hipertermic IntraPEritoneal Chemotherapy) in survival.There are two technically opposite techniques: CLOSED and OPEN, with several variations to enhance the safety and effectivity.In our hospital, we use CLOSED TECHNIQUE with CO2 RECIRCULATION; this recirculation optimizes the intraabdominal distribution of the chemotherapy agent while maintaining the virtues of original closed technique. We present our TECHNIQUE, with a thoracoabdominal variation (HITAC: Hipertermic ThoracoAbdominal Chemotherapy), RESULTS, and SECURITY.

Methods

When we started our program, developed a new database in Access 2013, with more than 400 items per patient.

Characteristics: PROSPECTIVE, 64 months, 89 patients with peritoneal carcinomatosis, evaluated in a Multidisciplinary Oncologic Committee and included in multimodal treatment protocol. 73 cytoreductions with HIPEC/HITAC.

Statistical analysis has been done with SPSS 25.

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Results

Tumour origin: COLON (33), STOMACH (24), LIPOSARCOMA (1), OVARY (10).Technique and HITAC variation: as shown in figure.SURGERY: COMPLETE CYTOREDUCTION in 94’4% of patients.Clinical PCI (presurgery): 5'33 ± 11’58.Intraoperative PCI: 6'47 ± 13'05.NO INTRAOPERATIVE DEATHS.NO CHEMOTHERAPY LEAKS or professional exposures.One patient (1’4%) showed INTRAOPERATIVE ALLERGY TO CHEMOTHERAPIC AGENT OXALIPLATIN.

PERIOPERATIVE PERIOD (30 days following surgery): Only ONE perioperative death on the 2nd day, a male of 40 years died after a massive pulmonary embolism.

EXTERNAL CONSULTING FOLLOWING

There is no evidence of recurrence in 61'1% of patients.MEDIAN SURVIVAL of 20'22 (±23'6) months.A 22'2% of patients has died.

GROUPED MORTALITY and MORBILITY (as classified by Clavien and grouping intra and postoperative periods):

NO complications: 32 (47’1%).

COMPLICATIONS: 36 (52’9%). Clavien III/IV: 8 patients (11%).

PERIOPERATIVE MORTALITY: 1 patient (1'4%).

MORTALITY IN FOLLOWING: 16 patients (21'9%).

Conclusion

1. HIPEC and HITAC are, today, safe procedures, with ACCEPTABLE INTRAOPERATIVE AND POSTOPERATIVE type and number of complications.

2. HITAC technical variation has not been shown to have specific thoracic complications in our patients; thus, the inclusion of THORACIC CAVITY in the setting is feasible and does not further increase complications.

C103

SURVIVAL AFTER SURGICAL EXPLORATION FOR INTENDED HIPEC PATIENTS WITH EXTENDED DISEASE

J.A. Funder, L. Hommelgaard, M.M. Sørensen, L.H. Iversen, V.J. Verwaal

Dept. of Surgery, Aarhus University Hospital - Aarhus (Denmark)

Objectives

Cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC) is the only treatment with curative intent for peritoneal metastases of colorectal or appendiceal cancer origin. However, if the peritoneal disease is unresectable or distributed to more than five out of seven regions a curative outcome from HIPEC

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is unlikely. To avoid complications and therewith delay palliative chemotherapy it is common practice to close these patients without performing major surgery if CRS and HIPEC is not feasible. The aim of this study is to describe outcome after “open-close” procedure.

Methods

From January 2014 to December 2017, we planned 218 CRS and HIPEC procedures colorectal or appendiceal cancer at Aarhus University Hospital, among whom 39 colorectal cancer patients with confirmed peritoneal metastasis underwent “open-close” procedures. All patients were evaluated before surgery at a multidisciplinary team conference and found eligible for CRS and HIPEC. Patients were prospectively registered, while perioperative data after “open-close” procedures were collected retrospectively from patient records.

Results

Among 39 patients with “open-close” procedures, 31 (80%) were evaluated before surgery with a laparoscopy. At laparotomy seven patients were excluded from CRS and HIPEC due to unresectable central disease. Two patients had extra-regional metastatic lymph nodes and the majority of patients (n = 27) were excluded due to widespread peritoneal spreading. Three patients were excluded on more than one parameter. Median PCI was 16 (range 2–30). The majority of patients (n = 22) received no additional surgery to the “open-close” procedure. Ten patients received an omentectomy (26%). Fourteen patients (36%) received additional surgery. Median operative time was 71 min (range: 28–230 min). Median hospital stay before discharge or transferal to local hospital was 2 days (1–9 days). In total, 38 (97%) patients had none or only Clavien-Dindo grade I complications at our department whereas one patient experienced Clavien-Dindo grade II complications (3%). Median follow-up was 16 months (1.4–39.5). Thirty-day mortality was 0%. Median survival was 20 months (1.4–39.5).

Conclusion

Outcome after “open-close” procedures is not associated with major morbidity. Therefore, an explorative laparotomy is probably is not worsening the outcome for those patients with marginal resectable disease in an attempt to perform a HIPEC.

C104

SAFETY OF BIDIRECTIONAL CHEMOTHERAPY WITH DIANEAL AS CARRIER FLUID IN AN EXPERIENCED CENTRE

J.F. Funder, L.H. Iversen, M.M. Sørensen, V.J. Verwaal

Dept. of Surgery, Aarhus University Hospital - Aarhus (Denmark)

Objectives

Previously, a protocol of bidirectional chemotherapy with leucovorin and 5FU systemic administered and oxaliplatin as HIPEC agent was launched. In this protocol Dianeal instead of glucose was used as carrier fluid. The stability of oxaliplatin in this solution and the electrolyte safety was tested and published before. In this study, we look at the overall safety when using Dianeal in a high volume centre with more than 10 years experience with CRS and HIPEC.

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Methods

Between October 2016 and January 2018, a total of 64 patients (37 males/27 females) underwent a HIPEC with the above mentioned bidirectional protocol. This was 57% of the total number of patients who underwent CRS and HIPEC in this period. Inclusion was peritoneal metastases of colon or rectal cancer. Exclusion was toxicity after prior oxaliplatin treatment.

Basic characteristics and in-hospital postoperative complications graded according to Clavien-Dindo were collected in the hospital quality control database and analysed.

Results

Median PCI of the 64 patients was 6 (range 0 to 18). The median age was 63 (range 32 to 78). Out of these 64 patients 48 (79.2%) had no complication above grade 2. The median hospital stay in the HIPEC centre was 10 days (range 7 to 19). Of the patients with complications, 5 had an anastomotic se or bowel leakage, which required reoperation, 4 had a wound dehiscence, 2 had an abscess that required drainage; 2 had a hernia and one received a chest tube because of pleura fluid. The median stay in the centre was 15 days (range 8–118). None of the patients had bleeding complications and no patients had electrolyte disturbances.

Conclusion

The majority on the fast patients had no complications. Of those who had complications this was due to the surgery. There was a remarkable high incidence of wound healing problems. We found no toxicity above grade 2 which was related to the chemotherapy or the perfusion fluid. Complications had a major impact on the hospital stay.

These data verifies that the described protocol is safe in an experienced centre.

C105

INTEROBSERVER AND INTERLABORATORY VARIABILITY IN THE REPORTING OF PT4A IN COLON CANCER

C. Klaver[1], N. Bulkmans[2], P. Drillenburg[3], H. Grabsch[4], N. Van Grieken[5], A. Karrenbeld[6], L. Koens[1], I. Van Lijnschoten[7], J. Meijer[8], I. Nagtegaal[9], X. Sagaert[10], K. Seldenrijk[11], M. Van Velthuysen[12], L. Overbeek[13], P. Tanis[1], P. Snaebjornsson[14]

[1]AMC - Amsterdam (Netherlands), [2]Spaarne Gasthuis - Haarlem (Netherlands), [3]OLVG - Amsterdam (Netherlands), [4]MaastrichtUMV - Maastricht (Netherlands), [5]VUmc - Amsterdam (Netherlands), [6]UMCG - Groningen (Netherlands), [7]PAMM - Eindhoven (Netherlands), [8]Rijnstate - Arnhem (Netherlands), [9]Radboudumc - Nijmegen (Netherlands), [10]UZ Leuven - Leuven (Belgium), [11]Antonius Ziekenhuis - Nieuwegein (Netherlands), [12]Erasmus MC - Rotterdam (Netherlands), [13]PALGA - Houten (Netherlands), [14]AVL - Amsterdam (Netherlands)

Objectives

T4 stage in colon cancer becomes increasingly important as a parameter on which therapies, including induction therapy, extent of (multivisceral) surgery, adjuvant therapy (HIPEC, duration of chemotherapy) and follow-up regimen are based. The aim of this study was to evaluate intra- and interobserver variability of

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diagnosing pT4 colon cancer, focussing on the challenging distinction between pT4a (peritoneal penetration) and deeply invasive pT3 stage, and their association with the number of tissue blocks taken from the tumour.

Methods

Part 1) Twelve pathologists were asked to classify 66 slides as pT3 or pT4a. Inter- and intraobserver variability were calculated using Kappa statistics.Part 2) For interlaboratory variability analysis pathology reports of pT3 and pT4a colon cancers (diagnosed between 2012 and 2015) were extracted from the Dutch PALGA database. After adjustment for case mix, percentages of pT4a diagnoses (pT4a/pT3+pT4a) were compared between laboratories.Part 3) From the part 2 patient group, those who developed metachronous peritoneal metastases (PM) were identified. The average number of blocks taken from pT3 and pT4a tumours for microscopic analysis was examined.

Results

Part 1) The intraclass correlation coefficient (ICC) was 0.50 (95%CI 0.41–0.60) (moderate agreement). Seven pathologists re-evaluated the slides, the median Cohen's kappa for intraobserver variability was 0.75 (range 0.43–0.93) (substantial agreement).Part 2) 7745 pT3/pT4a M0 colon cancer cases reported by 33 laboratories were included. The median percentage of pT4a cases per lab was 15.5% (reference lab) (range 3.2–24.6%). After adjustment for case mix, 8 labs (24.2%) significantly differed in diagnosing pT4a from the reference lab (in one lab pT4a was diagnosed more and in seven labs less frequently).Part 3) 299 out of 7745 (3.8%) patients developed metachronous PM. The mean number of blocks taken from the primary tumour was 4.03 (SD 1.51) in pT3 colon cancers, significantly less than 4.78 blocks (SD 1.76) in pT4a colon cancers.

Conclusion

We conclude that there is a substantial variability in diagnosing pT4a, both at a pathologist and a the laboratory level. Metachronous PM in pT3 patients might be related to understaging due to inadequate sampling. With the increasing importance of the pT4a category in clinical decision making pathologists need to aim at establishing standardized criteria for pT3/pT4a assessment.

C106

ABDOMINAL WALL METASTASIS IN PATIENTS WITH PERITONEAL METASTASIS OF COLORECTAL CANCER TREATED WITH CRS+HIPEC

E. Wassenaar[1], F. Hoogwater[2], R. Wiezer[1], D. Boerma[1], B. Van Ramshorst[1]

[1]St. Antonius Hospital - Nieuwegein (Netherlands), [2]University Medical Center Groningen - Groningen (Netherlands)

Objectives

The tumor biology and dissemination pattern of abdominal wall metastasis (AWM) is unknown. The aim of this study is to investigate whether cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS+HIPEC) is a beneficial option for patients with peritoneal metastasis form colorectal cancer (CRC-PM) and abdominal wall metastasis (AWM).

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Methods

The characteristics of patients with pathologically proven CRC-PM treated with CRS+HIPEC, with and without AWM, between 2005–2017 in a tertiary referral center, were analyzed. Main outcomes were overall survival (OS), disease-free survival (DFS) and recurrence patterns. Survival analysis was performed with a cox proportional hazard model.

Results

Fifty-four patients (23%) out of 234 CRC-PM patients underwent resection for AWM during or after the CRS+HIPEC procedure. Median OS was 24,1 months (IQR 13,4–49,5) in the AWM-group versus 22,1 months (IQR 11,9–40,1) in the non-AWM-group (p = 0,28). Median DFS was 11,8 months (IQR 5,9–19,1) in the AWM-group versus 11,9 months (IQR 6,0–22,3) in the non-AWM-group (p = 0,88). The combination of peritoneal and abdominal wall metastasis did not influence OS or DFS in the cox protortional hazard model (for OS HR 0,85 95%CI 0,54–1,34 and for DFS HR 1,06 95%CI 0,72–1,55). After AWM resection during CRS+HIPEC, recurrent disease was primarily intraperitoneal (45% of all recurrence cases), followed by liver (24%), lung (13%) and abdominal wall (13%). In the non-AWM-group, this was respectively 46%, 12%, 20%, and 13%.

Conclusion

The colorectal cancer outcome of patients with both AWM and peritoneal metastasis is fairly similar to the outcome of solely peritoneal metastasis in colorectal cancer. Therefore, abdominal wall metastasis is not an exclusion criteria for a curative treatment intent with CRS+HIPEC for patients with CRC-PC.

C107

SYSTEMATIC REVIEW OF PROTOCOLS USED FOR HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) AFTER CYTOREDUCTIVE SURGERY OF PERITONEAL METASTASIS FROM COLORECTAL CANCER

C. Yurttas[1], G. Hoffmann[1], S.P. Haen[2], A. Königsrainer[1], S. Beckert[1], M.W. Löffler[1]

[1]University Hospital Tübingen, Department of General, Visceral and Transplant Surgery - Tuebingen (Germany), [2]Internal Medicine, Department for Oncology, Hematology, Immunology, Rheumatology and Pulmonology, University of Tübingen - Tuebingen (Germany)

Objectives

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is an effective treatment for peritoneal metastasis combining radical surgical intervention with local heated chemotherapy in colorectal cancer (CRC). The contribution of HIPEC, however, remains unclear, since standardized and therefore comparable HIPEC procedures are lacking.

Methods

A systematic scientific literature search was performed using the keywords “HIPEC” and “colorectal cancer” in PubMed accordant with PRISMA guidelines. In total 397 articles published until 01/2017 were screened, selecting 87 publications for synthesis and further evaluation and complemented with 48 publications identified through manual snowballing search and extracting information on HIPEC conduct, drugs, applied dosages, exposure time and carrier solutions used.

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Results

From these 135 publications, we extracted reports on 171 HIPEC protocols with at least twenty distinct ways of dosing for the most frequently used drug mitomycin C (MMC) alone, describing slight to considerable differences. Besides the most frequently used drugs MMC and oxaliplatin, various other drugs and drug combinations are in used, as well as a wide range of drug dosages (benchmarked in mg; mg/kg; mg/l; mg/m² or mg/m²/l) and exposure times from 0.5 to 2 h.

Conclusion

Insufficient information on drug administration and lacking comparability between dosage benchmarks are an obstacle preventing meaningful comparisons between HIPEC interventions and inhibit scientific discourse and meta-analyses. We therefore advocate indicating final drug concentrations as a future standard benchmark to establish comparability in HIPEC.

C108

PERITONEAL METASTASIS (PM) FROM COLONIC ORIGIN. 423 PATIENTS TREATED BY CRS+ HIPEC. CATALONIAN PERITONEAL CARCINOMATOSIS PROGRAM (SPAIN)

I. Ramos Bernadó, P. Barrios Sanchez, O. Crusellas Maña, M. Martín Baranera, D. Sabia

Consorci Sanitari Integral. Hospital de Sant Joan Despí, Moisès Broggi. Carcinomatosis Peritoneal Program. - Barcelona (Spain)

Objectives

25% of colon cancer patients will present peritoneal metastases (PM) during follow up. Recent studies in selected group of patients with colorectal PM, treated with CRS+HIPEC and postoperative chemotherapy, report 5-y survivals (OS) of 30–52%. Correct patient selection and surgical team experience are determining factors in the efficacy and safety of radical treatment, currently considered the standard treatment. Extensive series of patients treated homogenously allow to define survival independent prognostic factors. We present the experience and results of a PM national treatment program.

Methods

September06/ March18: 898 patients with PM from different types of Peritoneal Surface Malignancies have been treated by 1000 CRS+HIPEC procedures; 423 had carcinomatosis from colon tumors. Rectum PM and appendiceal PM (non PMP) have been excluded from this series.

CRS was achieved using peritonectomy procedures and HIPEC using oxaliplatin (48%) or irinotecan (35.6%), 42°C, 30 min. Bidirectional chemotherapy: iv 5FU plus Folinic acid, 1 hr before HIPEC.

Kaplan-Meier curves and Log-Rank tests have been applied to assess the relationship between overall survival and several clinical, surgical and anatomopathological factors.

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Results

Female: 222, Male: 199. Mean age 59.3 years. Mean PCI: 7.14 /39. CC0: 93.1%.

Median operative time: 306.5 min. Median ICU and hospital stay: 2 and 11 days.

Overall morbidity: 30.3%. G3-4: 21.1%. Reintervention: 5.7%. 30-day mortality rate: 0.1%. Readmissions after hospital discharge: 4.3%.

Mean follow up: 29.6 m. (1–131). Cumulative survival probability at 12 months: 93.1%, 3 y: 57.9%, 5 y: 34.1%.

Mean/ median overall survival of 57.17/ 40.59 m.

From all analyzed items we describe some with influence on the results:

PCI <10 OS 49.57 m, PCI 10–20 OS 31.21 m, PCI 21–30 OS 23.38 m,

CC0 41.65 m, CC1 25.69 m, CC2-3, 12.27 m,

Classic adenocarcinoma 42.76 m, mucinous adenocarcinoma 31.27 m,

Signet ring cells, 19.3 m, absence 41.84 m. Histologic grade 1–2: 40.92 m, Gr 3: 27.4 m,

PSDS 2–3: 61.38 m, PSDS 4–7: 39.40 m, PSDS 8–10: 27.46 m.

Conclusion

CRS+HIPEC with systemic adjuvant chemotherapy is considered the standard treatment for PM from colonic origin. Well-known prognostic indicators of improved survival include low to moderate PCI (<21/39) and a complete radical surgery. The selection aim is to achieve median survival rates above 35 m.

C109

PERITONEAL METASTASIS (PM) FROM GASTRIC ORIGIN. 45 CONSECUTIVE PATIENTS TREATED WITH RADICAL CYTORREDUCTION AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (CRS+HIPEC). RESULTS FROM THE CATALONIAN PERITONEAL CARCINOMATOSIS PROGRAM (SPAIN)

D. Sabia, I. Ramos Bernadó, O. Crusellas Maña, M. Martín Baranera, P. Barrios Sanchez

Consorci Sanitari Integral. Hospital de Sant Joan Despí, Moisès Broggi. Carcinomatosis Peritoneal Program. - Barcelona (Spain)

Objectives

PM from gastric origin is associated with poor survival, with mean survival from 3 to 9 months, and 0% survival at 5 y. Systemic chemotherapy offers little benefit in symptoms control and survival. CRS+HIPEC has a beneficial impact in selected patients with gastric PM, with significant statistically benefit in overall survival. We present the results of patients with PM from gastric origin treated with CRS+HIPEC at a highly specialized center.

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Methods

Sept'06/Mar'18: 898 pt with PM from different types of Peritoneal Surface Malignancies have been treated by 1000 CRS+HIPEC procedures. Of those, 45 pt had gastric PM.

F:27, M:18. Mean age: 52.4 y.

35 pt had synchronous PM y 10 metachronous PM. Positive cytology was the indication in 6 pt.

Histology: 14 pt diffuse adenoacrcinoma, 28 pt intestinal, 1 pt mucinous and 23 pt signet ring cell.

Mean PCI: 6/39. CRS: CC0 in 41 pt and CC1 in 4.

30 total gastrectomies and 4 subtotal gastrectomies.

Reconstruction: 21 Henley-Longmire, 8 Y-Roux, 6 Billrtoth II.

HIPEC with CDDP+Doxorrubicin at 42.5°C, 60 min.

Mean operative time: 372 minutes.

Median ICU and Hospital stay: 2 and 14 days.

Results

Ours results, showed in this series, have been subjected to an external audit.

Median follow-up: 12.6 months (1.9–109.6 months).

Grade III-IV morbidity: 24.4%. No anastomotic leaks.

Mortality: 0%.

Mean/ Median survival: 31.2/20.6 m.

Median survival PCI ≤ 10 vs >10 was 27.1 vs 8.1 m.

Median survival signet ring cell vs absence: 12.5 vs 32.1 m.

Conclusion

CRS+HIPEC is highly recommended for PM from gastric carcinoma, in a selected group of patients. Good response to prior systemic therapies, low PCI (≤10/39), complete cytorreduction surgery and favorable histological grade are prognostic factors used for patient selection at our Program. It is especially important to refer these patients to a specialized center as soon as possible.

C110

ITERATIVE CRS+HIPEC PROCEDURES (IHIPEC). EXPERIENCE AND RESULTS OF THE PERITONEAL CATALONIA CARCINOMATOSIS PROGRAM (SPAIN)

I. Ramos Bernadó, D. Sabia, O. Crusellas Maña, M. Martín Baranera, P. Barrios Sanchez

Consorci Sanitari Integral. Hospital de Sant Joan Despí, Moisès Broggi. Carcinomatosis Peritoneal Program. - Barcelona (Spain)

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Objectives

CRS+HIPEC provides increasingly broad survival to selected patients with peritoneal metastases (PM). Best results are achieved when treatment is performed on patients in favorable clinical situations such as small volume of peritoneal involvement (low PCI) and complete cytoreduction, especially CC0. A significant percentage of patients undergoing CRS+HIPEC recur as peritoneal disease. Safety in application of treatment has promoted its repeated use in exclusive peritoneal recurrence. Indication of iterative CRS+HIPEC (iCRS+HIPEC) is carried out under demanding selection criteria: low PCI, completeness of cytoreduction (CC0), biology and natural history of disease, general condition and absence of major comorbidity. We present our institution's experience in iCRS+HIPEC.

Methods

From September 2006 to March 2018, 898 patients underwent 1000 CRS+HIPEC procedures, for different types of PM. 102 iCRS+HIPEC were performed in 87 patients; 65 females and 22 males. Mean age 56 years. 29 patients had recurrent colon PM, 28 recurrent peritoneal pseudomyxoma, 5 recurrent appendicular tumor PM, 18 recurrent ovarian tumorPM, 4 recurrent malignant peritoneal mesothelioma, 2 recurrent sarcomatosis and one patient treated for gastric PM and later on for colon PM.

Results

Mean PCI: 8. CC0 81.6%, CC1 10.3, CC2 6.8% and CC3 1.1%. Mean surgical time was 318 minutes. Median hospitalization: 10 days. Time between initial and iterative CRS+HIPEC was 25.6 months.

Overall morbidity: 28.7%. G3-4 17.2%. Reoperation 4 patients. Mortality: 0%. Follow up: 25 patients died, 62 stay alive. 31 without disease, 31 with disease (5 with localized disease, 21 with diffuse peritoneal disease and 21 with disseminated disease). Median follow-up was 60 months. Overall mean survival was 101 months and 5-year survival was 79.9%. By PM's origin, mean survival was 124, 84.5 and 79.3 months for pseudomyxoma, recurrent ovarian cancer and colon cancer respectively. By PM's origin, the 5-year survival was 91.9%, 85.6% and 63.7% for pseudomyxoma, recurrent ovarian cancer and colon, respectively.

Conclusion

iCRS+HIPEC doesn't show higher rate of complications than initial radical treatment of PM. It can be performed with 0% mortality and provides a significant increase in patients' survival.

In our opinion, best candidates for iCRS+HIPEC are: Free survival period: more than one year, low PCI with completely resectable disease, non-aggressive tumor histology, absence of extra-abdominal disease and good performance status.

C111

1000 CRS+HIPEC PROCEDURES. EFFICIENCY AND SAFETY RESULTS

I. Ramos Bernadó, D. Sabia, O. Crusellas Maña, M. Martín Baranera, P. Barrios Sanchez

Consorci Sanitari Integral. Hospital de Sant Joan Despí, Moisès Broggi. Carcinomatosis Peritoneal Program. - Barcelona (Spain)

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Objectives

CRS+HIPEC is a multimodal aggressive treatment usually performed on multitreated and weakened patients with a potential risk of complication. From this description a number of objections to its use have raised: results of Sugarbaker difficult to reproduce, limited levels of evidence, highly aggressive, complex and expensive therapy, negative repercussions on the quality of life as well as an outrageous morbi-mortality rates. Despite this, it is the current standard treatment in different types of peritoneal metastasis.

We describe the results of a Peritoneal Carcinomatosis Program (a territorial centralized, highly specialized and with government funding model with particular reference to complications.

Methods

September2006/ March2018: 1000 CRS+HIPEC (898 patients). 326 men and 568 women. Average age: 57.2 years (range 22–83).

423 patients had peritoneal metastasis (PM) from colon cancer, 176 pseudomyxoma peritonei, 120 recurrent ovarian cancers, 45 gastric, 36 appendiceal tumors, 24 malignant peritoneal mesotheliomas, 23 rectum cancers, 10 peritoneal sarcomatosis, 7 small bowel and 34 other pathologies.

Previous chemotherapy: 76.4%. Previous surgery: 90,6%. Regions affected: 5/13. PCI: 10/ 39.

Associated visceral involvement: 65%. CC0-1: 96.5%. HIPEC (Coliseum technique) with drugs and exposure time related to the type of PM. Mean surgical time: 5 h 40 m.

Results

Morbidity: 31.9%. GIII-IV: 17.2%. Most frequent complications hemoperitoneum, abdominal collection and central line infection. Reoperation: 5.9%. Most frequent cause of reoperation hemoperitoneum and intestinal occlusion. Median ICU stay: 2 d. Median hospital stay: 12 d. Readmissions after hospital discharge: 6%. Mortality: 0.2% (2p).

Follow-up: mean 34.2 months (range 1–149.28 m). Cumulative probability of survival (12–36–60 m): 91.4–62.1–44.5%. Median survival: 48.7 m.

Colon: OS 40.5 m. Pseudomyxoma peritonei: OS 109 m. Recurrent ovarian cancer: OS 45.36 m. Gastric: OS 20.62 m. Appendiceal: OS 34.9 m. Mesothelioma: OS 62.7 m. Rectum: OS: 27.3 m.

Conclusion

Surgery is the treatment’s keystone. Right surgical indication, right technical realization and postoperative care determine clinical results, especially complications, of Sugarbaker’s technique.

Accurate planning, development and implementation of a specialized program in the management of PM, in conjunction with the scientific and technical training of the surgical team, are the guarantee of efficiency and safety of this procedure.

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C112
AND HIPEC FOR GASTRIC COUTCOME IN PATIENTS TREATED WITH CYTOREDUCTIVE SURGERYANCER AND PERITONEAL CARCINOMATOSIS

F.B. Braeuer, H.W. Wundsam, F.B. Fischer, G.P. Pressl, R.F. Fuegger, K.R. Rohregger

Congregation Hospital Linz, Mercy Sisters - Linz (Austria)

Objectives

Gastric cancer remains one of the most aggressive malignancies with poor prognosis, especially in patients with advanced disease. Patients with peritoneal carcinomatosis originating from gastric cancer have a median overall survival rate below one year. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) display promising data improving overall survival (OS) and disease-free survival (DFS).

Methods

We performed a retrospective analysis of patients treated with gastric cancer with stage UICC ≥ III at our department from January 2012 to September 2017. The collective was grouped accordingly UICC stage. We compared the outcome concerning OS and DFS of patients with UICC III to patients with UICC IV treated with CRS and HIPEC to UICC IV without CRS and HIPEC.

Results

One hundred patients have been included in this analysis. In group 1 (UICC III), we analysed 38 patients with a two-year OS rate of 47,7%. In comparison, patients of group 2 (UICC IV with CRS and HIPEC, n = 8) showed a two-year OS rate of 70%. The PCI in this group ranged from 1 to 7. The two-year OS rate of patients with UICC stage IV (group 3, n = 54), who were not treated with HIPEC, was 11,3%.

Conclusion

CRS and HIPEC show promising results improving overall survival of patients with peritoneal carcinomatosis from gastric cancer and a low PCI score (<8).

The benefits of prophylactic HIPEC have already been demonstrated in peritoneal carcinomatosis from colorectal cancer. Therefore, we should ascertain risk factors for patients with gastric cancer stage UICC III and assess, if prophylactic HIPEC improves DFS as well as OS in this group.

C113
CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY: A SINGLE-CENTER EXPERIENCE IN PORTUGAL

C. Fernandes, J. Simões, F. Sousa, V. Devezas, S. Meireles, C. Sarmento, M. Aral, T. Machado, R. Melo, J. Costa-Maia

Centro Hospitalar São João - Porto (Portugal)

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Objectives

Peritoneal surface malignancy (PSM) represents advanced disease and, generally, is associated with a poor prognosis. Although PSM is categorized as metastatic disease, it represents a special dissemination pattern considered to be locoregional disease limited to the abdominal cavity. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) have been used as locoregional treatment for selected patients with PSM and have shown survival's improvement. Therefore it can be considered as being standard of care for primary disease and (limited) disease from other origins. Our aim was to present the experience of our institution in treating oncologic patients with CRS and HIPEC.

Methods

Retrospective analysis of patients treated with CRS and HIPEC between July 2010 and December 2017 at our institution. Survival analysis was performed using Kaplan-Meier method and prognostic factors assessed by univariate analysis and by Cox regression model.

Results

This single-center analysis included all patients (n = 61) with PSM from various origins selected to CRS and HIPEC: colorectal (n = 22; 36.1%), appendix (n = 14; 23%), ovarian (n = 12; 19.7%), gastric (n = 6; 9.8%), peritoneal (n = 5; 8.2%), small bowel (n = 1; 1.6%) and Fallopian tube (n = 1; 1.6%). Five patients had repeated CRS and HIPEC due to isolated and limited peritoneal recurrence. The median age at diagnosis of oncologic disease was 53 years (20–74) and 67% were women. Eastern Cooperative Oncology Group (ECOG) Performance Status was 0 in 90% of patients. Regarding the histological type – 51% of patients had adenocarcinoma, 21% mucinous adenocarcinoma, 16% serous papilar adenocarcinoma, 8% pseudomyxoma peritonei and 2% mesothelioma. Eleven patients had non-resectable disease. Median operating time was 550 minutes (354–870). The most used intraperitoneal chemotherapy was cisplatin plus mitomycin (38%). Twelve (19.7%) patients experienced Dindo-Clavien grade III/IV complications and postoperative 90-day mortality was 3%. Five-year overall survival (OS) was 47.6% with a cytoreduction completeness (CC) score of 0/1 in 51%.

Conclusion

Due to strict inclusion and exclusion criteria and meticulous preoperative patient evaluation, we were able to achieve an excellent 5-year OS of 47.6%. Our results demonstrate the feasibility, efficacy and safety of CRS and HIPEC.

C114

RECTAL RESECTION DOES NOT INCREASE THE MAJOR MORBIDITY IN PATIENTS UNDERGOING CRS AND HIPEC FOR COLORECTAL PM- A REPORT FROM THE INDIAN HIPEC REGISTRY

S. Mehta[1], P. Kammer[2], S. Zaveri[3], D. Damodaran[4], M. Ray[5], S. Sinukumar[6], R. Seshadri[7], A. Bhatt[8]

[1]Saifee Hospital - Mumbai (India), [2]Global Hospital - Hyderabad (India), [3]Manipal Hospital - Bangalore (India), [4]MVR Cancer Institute and Research Center - Calicut (India), [5]All India Institute of Medical Sciences - New Delhi (India), [6]Jehangir Hospital - Pune (India), [7]Cancer Institute (WIA) - Chennai (India), [8]Zydus Hospital - Ahmedabad (India)

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Objectives

To study the impact of rectal resections on grade 3–4 morbidity in patients undergoing cytoreductive surgery and HIPEC for colorectal peritoneal metastases.To evaluate the impact of a diverting stoma on morbidity.

Methods

A retrospective analysis of patients with colorectal PM enrolled in the Indian HIPEC registry from March 2016 to December 2017 was performed.

A comparison of grade 3–4 morbidity and anastomotic leak rate in patients with and without a rectal resection was performed. A comparison was also made between patients with and without a diverting stoma.

Results

Of the 68 patients undergoing CRS and HIPEC, 25 had a rectal anastomosis (RA), 20 had a non-rectal anastomosis (NRA) and 23 patients had no bowel anastomosis.

In the RA group, 10 (25.0%) patients had two anastomoses (small bowel/colonic) and in the NRA group 2 (10%) patients had two bowel anastomoses. A diverting stoma was created in 7 (28%) patients in the RA group and in 3 (15%) patients in the NRA group. All patients with a rectal anastomosis below the peritoneal reflection received a diverting stoma.

Overall grade 3–4 morbidity was seen in 29.4% patients and 2 (2.9%) patients died within 90 days of surgery due to complications. A PCI > 20 was the only predictor of increased grade 3–4 morbidity. Grade 3–4 complications occurred in 40% patients with RA, 30% with NRA and 17.3% patients without any bowel anastomosis ($p = 0.22$). In both RA and NRA groups, with either 1 or 2 bowel anastomosis, a diverting stoma was not associated with a reduced risk of morbidity ($p = 0.58$ and $p = 0.37$ for 1 and 2 anastomosis, respectively).

3 patients had anastomotic leaks in the RA group. All the leaks occurred in patients who did not have a stoma and from the rectal anastomosis. No anastomotic leaks occurred in the NRA group; however, 2 patients developed bowel fistulas. Of the 3 patients who had a leak, two had prior pelvic surgery and received one or more lines of chemotherapy; the third patient had prior surgery and 2 lines of chemotherapy. All 3 patients had a PCI >12.

No mortality was observed in patients having bowel related complications. Age greater than 65 and systemic toxicity were the independent predictors of 90-day mortality.

Conclusion

Rectal resection does not significantly increase the grade 3–4 morbidity in patients undergoing CRS and HIPEC for colorectal PM. A diverting stoma can be avoided in selected patients with a rectal anastomosis at low risk of complications without increasing the morbidity.

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C115
CRS AND HIPEC IN THE ELDERY

A. Nissan[1], A. Bilik[1], J. Dux[1], A. Ben-Yaacov[1], D. Perlson[2], D. Zippel[1], V. Ivanov[3], S. Yehuda[3], G. Schtrechman[1], T. Kaplun[1], A. Al-Kurd[4]

[1]Sheba Medical Center, Surgery C Department - Ramat Gan (Israel), [2]Sheba Medical Center, Anesthesiology Department - Ramat Gan (Israel), [3]Sheba Medical Center - Ramat Gan (Israel), [4]Hadassa Medical Center - Jerusalem (Israel)

Objectives

Worldwide there has been an increase in the overall life expectancy leading to an increase in the elderly population. The incidence of cancer is known to increase with age, consequently, the incidence of patients with peritoneal metastases. This study was designed to review the clinical outcomes in elderly patients who underwent CRS and HIPEC.

Methods

Prospectively collected database of patients undergoing CRS/HIPEC was reviewed. All Patients divided into 3 age groups: young (<60), intermediate (60–75) and old (>75). Patient's demographics, short term (peri-operative) and long-term (survival) outcomes were compared between the study group (>75) and the control group (<60). The intermediate age group (n = 101) was excluded. Clavien Dindo (CD) 5- tiered score was used to report post-operative complications. In order to predict the risk for complications, logistic regression was conducted. To examine difference in overall (OS) and Disease Free Survival (DFS), between groups, the Kaplan-Meire product limit method was used.

Results

Out of 352 patients, HIPEC was performed in 276 patients (77.5%). Study group (>75 years) included 10 patients, control group (<60 years) included 165 patients. Higher rates of comorbidities were found among the study group compared to the control group (63.0% vs. 20.0%, respectively, p = .004). No significant differences were found in terms of primary diagnosis, EBL, PCI, OR time and CC score. Short term outcomes including ICU stay, hospital stay and complications were the same. Logistic regression showed no difference between age groups in achieving CC 0–1 (OR = 0.755, 95% CI 0.138–4.142, p = 0.746). Results demonstrated that longer OR time was positively correlated with CD score (OR = 1.201, 95% CI 1.007–1.432, p = .041). OS and DFS were the same in both groups (5-year OS was 60% for study group and 65% for control p = .993).

Conclusion

Carefully selected patients older than 75, can tolerate CRS/HIPEC with a good long-term outcome.

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C116
NEOADJUVANT BIDIRECTIONAL CHEMOTHERAPY COMBINING INTRAPERITONEAL DOCETAXEL WITH INTRAVENOUS 5-FLUOROURACIL AND OXALIPLATIN FOR PATIENTS WITH NON-RESECTABLE PERITONEAL CARCINOMATOSIS FROM GASTRIC CANCER: THE FIRST PILOT STUDY IN WESTERN COUNTRIES

R. Lo Dico[1], J.M. Gornet[2], N. Guglielmo[3], F. Bart[4], A. Zaanan[5], J. Taieb[5], M. Pocard[1]

[1]INSERM U965 Paris 7 Diderot University - Department of Oncological Surgery - Lariboisiere Hospital - Paris (France), [2]Department of Oncology - St Louis Hospital - Paris (France), [3]Department of Oncological Surgery - Lariboisiere Hospital - Paris (France), [4]Department of Anesthesiology - Lariboisiere Hospital - Paris (France), [5]Department of Oncology - HEGP Hospital - Paris (France)

Objectives

In patients with synchronous peritoneal spread from gastric cancer, only palliative treatment is proposed. Asiatic surgeons have shown encouraging results using bidirectional combination of intraperitoneal and intravenous chemotherapy with high response rate and low incidence of toxicity. We conducted the first pilot study in Western country, using bidirectional combination of European-standard drugs for gastric cancer. The main endpoint was to evaluate the feasibility and safety of this treatment. Secondary endpoint was success of therapeutic strategy reflected by overall survival (OS) and the decrease of 25% of attempted peritoneal cancer index (PCI) evaluated by laparoscopy.

Methods

Patients with non-resectable peritoneal carcinomatosis from gastric cancer underwent a bidirectional chemotherapy using intraperitoneal docetaxel and intravenous 5-fluorouracil (5FU) and oxaliplatin (FOLFOX). Docetaxel was administered at 30 mg/m^2 intraperitoneally at day 1, 8 and 15 and IV FOLFOX was administered intravenous at day 1 and 15 followed by 7 days rest, as one course. After three courses, the PCI was evaluated with a second laparoscopy. New bidirectional cycle of three months was proposed at patients with partial PCI response without major toxicity.

Results

We enrolled six consecutives patients. The average age was 47.1 years [range 24–66], performance status ECOG 0-1. The mean PCI was 34 (range 30–39). After one bidirectional cycle, major complications (grade 3/4) occurred in two patients (hematologic and asthenia). One patient had major PCI response, 3 partial PCI response and 2 clinical progressions. The mean PCI decrease to18 (range 12–29). Four patients had 2 bidirectional cycles and one had 3 bidirectional cycles. The median OS was 10.3 months (range 5–23); 1-year OS rate was 50%. One patient was operated with CC0 resection after major response.

Conclusion

This pilot study confirms the feasibility and safety of bidirectional treatment with IP and IV chemotherapy for patients with synchronous peritoneal carcinomatosis from gastric cancer, resulting in 10.3-months median OS with limited morbidity. The decrease of PCI after one bidirectional cycle is promising. Further phase I-II studies are required for the validation of this strategy.

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C117
CRS WITH HIPEC FOR PERITONEAL CARCINOMATOSIS OF PANCREATIC ADENOCARCINOMA. WHAT DO WE EXPECT? RESULTS OF A MULTICENTER INTERNATIONAL STUDY

L. Schwarz[1], E.A. Levine[2], D.L. Morris[3], J. Spiliotis[4], O. Glehen[5], D.L. Bartlett[6], M. Pocard[7], R. Kianmanesh[8], Y. Yonemura[9], P. Cashin[10], A.A.K. Tentes[11], L. Villeneuve[12]

[1]Department of digestive surgery, Rouen university hospital - Rouen (France), [2]Department of Surgical Sciences-Oncology, Wake Forest Baptist Medical Center - winston Salem (United States), [3]Department of Surgery, University of New South Wales, - Sydney (Australia), [4]First Department of Surgical Oncology, Metaxa Cancer Memorial Hospital - Piraeus (Greece), [5]Department of Digestive Surgery, Centre Hospitalier Lyon Sud, Pierre-Bénite - Lyon (France), [6]Department of Surgery, University of Pittsburgh Medical Center Shaydyside Hospital - Pittsburgh (United States), [7]Department of Surgical Oncology, Hospital Lariboisière, APHP - Paris (France), [8]Department of Digestive Surgery, Reims University Hospital - Reims (France), [9]NPO Organization to Support Peritoneal Dissemination Treatment, Kishiwada - Osaka (Japan), [10]Department of Surgery, Akademiska sjukhuset, Uppsala University Hospital - Uppasala (Sweden), [11]Didimotichon General Hospital Konstantinoupoleos 1 - Didimotichon (Greece), [12]Hospices Civils de Lyon, Pôle Information Médicale Evaluation Recherche, Unité de Recherche Clinique - Lyon (France)

Objectives

Even in the new era of FOLFIRINOX, the prognosis of peritoneal metastasis (PM) of pancreatic adenocarcinoma (PDAC) is poor. The value of metastasis resection and particularly of resection of peritoneal metastasis remains a matter of intense and controversial discussion. It is unclear whether combinations of extensive surgery, such as cytoreduction surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC), might confer a survival benefit particularly in younger and fitter patients.

Methods

An international multicentric cohort was constituted by retrospective analysis of 21 patients undergoing CRS/HIPEC for PM of PDAC between 1990 and 2015 from 10 reference centers of PSOGI. Data on clinical features, treatment strategies, and survival outcomes were analyzed.

Results

The median time interval from the diagnosis of PM to the procedure was 3 [0–39] months. The median peritoneal cancer index was 14 [6–22]. Fourteen patients had complete cytoreduction (CCR0-1). 9 patients had grades 3 to 4 complications. None died postoperatively. The median duration of follow-up was 16 months. The median OS was 13.9 months. The projected 1 y, 3 y and 5 y-OS were 60.8, 24.3% and 0% respectively. The median OS for patients with CCR0-1 was 24 months resection whereas it was 4 months for those with CCR2-3 resection after CRS ($p < 0.0001$). The median RFS was 13.2 months and projected 1 y and 3 y-RFS were 61% and 0%. With regard to prognostic factors for OS, the cytoreduction status (CCR0-1; $p = 0.0009$) and HIPEC with open technique ($p = 0.03$) have been found to be significant in the univariate analysis ($p = 0.0009$).

Conclusion

When a complete cytoreduction could be done, CRS/HIPEC could be discussed in highly selected patient in the setting of PM of PDAC, with prolonged better survival comparing with palliative chemotherapy.

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C118
CYTOREDUCTIVE SURGERY AND HIPEC – THE POLISH EXPERIENCE

T. Jastrzebski[1], W. Polkowski[2], W. Zegarski[3], M. Bebenek[4], P. Richter[5], T. Olesinski[6], T. Polec[1], B. Kapturkiewicz[7], J. Mielko[2]

[1]Surgical Oncology Department, Medical University of Gdansk - Gdansk (Poland), [2]Surgical Oncology Department, Lublin - Lublin (Poland), [3]Surgical Oncology Department, Oncological Center Bydgoszcz - Bydgoszcz (Poland), [4]Surgical Department, Lower Silesian Oncological Center - Wroclaw (Poland), [5]Surgical Department, Jagiellonian University, Medical Faculty - Kraków (Poland), [6]Oncological Center - Institut Sklodowskiej-Curie Memorial - Warszawa (Poland), [7]Surgical Department,Lower Silesian Oncological Center - Wroclaw (Poland)

Objectives

The first CRS with HIPEC procedure was performed in 1999 in Surgical Oncology Department, Medical University of Gdańsk. From that time peritoneal metastases are treated by this method in 7 surgical and oncological centers in Poland.

Methods

Currently there are 7 CRS and HIPEC centers: Surgical Oncology Department, Medical University of Gdańsk (2009), Surgical Oncology Department, Lublin (1010), Department of General Surgery Jagiellonian University Kraków (2011), Surgical Oncology Department, Oncological Center, Bydgoszcz (2013), General Surgery Department, Lower Silesian Oncological Center, Wrocław (2014), Oncological Center – Institut, Warszawa (2014), Oncological Surgery Department, Brzeziny Hospital (2015).

Standards for CRS and HIPEC procedures in colon cancer, pseudomyxoma peritonei and mesothelioma are included in guidelines of Polish Society of Clinical Oncology and Polish Society of Surgical Oncology, These guidelines are included to the surgical oncology specialization test. Despite the HIPEC is not a standard for peritoneal metastases of ovarian cancer, this type of neoplasm constitute about 50% all, treated patients.

The level of reimbursement of CRS and HIPEC are understated, but the works currently are in process in Polish Agency for Medical Technology and Tarriff, and to June 2018 cost assessment should be done.

Results

To May 2018 in all centers in Poland about 600 cytoreductive surgery with HIPEC procedures was performed. The main types of cancers qualificated to HIPEC were colon cancer, ovarian cancer, pseudomyxoma peritonei, gastric cancer, mesothelioma peritonei and primary peritoneal cancer. Rare case, such as gallbladder cancer, yolk sac tumour, seminoma composed only 0,03% of all cases.

The material and treatment results will be elaborated.

Conclusion

Surgical and oncological centers in Poland have great possibilities to treat patients with peritoneal metastases. Appropriate assessment and reimbursement cover real cost should be appeal to develop HIPEC procedure in Poland.

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C119
FAILURE TO RETURN TO INTENDED ONCOLOGICAL TREATMENT (RIOT) AFTER HIPEC IMPAIRS PROGNOSIS IN GASTRIC PERITONEAL CARCINOMATOSIS- ANALYSIS OF THE BIG-RENAPE GROUP

P.E. Bonnot[1], G. Passot[1], E. Decullier[2], F. Quenet[3], D. Goere[4], K. Abboud[5], M. Pocard[6], P. Meeus[7], J.M. Bereder[8], S. Msika[9], C. Arvieux[10], D. Pezet[11], P. Rat[12], R. Wernert[13], T. Courvoisier[14], N. Pirro[15], O. Glehen[1], F.J. Lacueva[16]

[1]HCL, Centre Hospitalier Lyon Sud, Digestive and surgical oncology - Lyon (France), [2]HCL,Pôle Information Médicale Évaluation Recherche - Lyon (France), [3]Department of Surgery, Institut Du Cancer de Montpellier - Montpellier (France), [4]Institut Gustave Roussy Villejuif, Department of Surgery - Paris (France), [5]CHU Saint-Etienne, Digestive and oncological surgery - Saint Etienne (France), [6]Hopital Lariboisiere AP-HP, Service de Chirurgie Digestive et Cancérologique - Paris (France), [7]Centre Léon Bérard, Department of Surgery - Lyon (France), [8]CHU NICE, Department of Digestive surgery - Nice (France), [9]Hopital Louis Mourier, AP-HP, Department of Surgery - Paris (France), [10]CHU Grenoble, Department of Surgery - Grenoble (France), [11]CHU Clermont Ferrand, Department of Surgery - Clermont Ferrand (France), [12]CHU Dijon, Department of Surgery - Dijon (France), [13]Institut de Cancérologie de l'Ouest Paul Papin, Department of Surgery - Angers (France), [14]CHU Poitiers, Department of Surgery - Poitiers (France), [15]CHU La Timone Marseille, Department of Surgery - Marseille (France), [16]Servicio de Cirugía General y Digestiva, Unidad Carcinomatosis Peritoneal, Hospital General Universitario de Elche - Elche (Spain)

Objectives

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) are associated with complications and disability that can prevent some patients from receiving subsequent adjuvant treatments. Inability to complete all intended adjuvant therapies might impair prognosis in survival terms. This study evaluated the Return to Intended Oncological Treatment (RIOT) rate, its impact on survival and risk factors that could prevent RIOT in patients who underwent CRS and HIPEC for gastric carcinomatosis (GC).

Methods

Outcomes for 136 patients who underwent CRS and HIPEC for GC and for whom adjuvant therapy was indicated, in 13 French institutions from 1989 to 2014, were examined. Morbidity events at 90-days were defined according to the NCI-CTCAE classification. The log-rank test was used to compare survivals and Cox models to identify risk factors.

Results

Of the 136 patients, only 86 could follow adjuvant therapy, yielding a RIOT rate of 63.2%. The remaining 50 (36.8%) were unable to RIOT due to surgical complications (n. 28), poor performance status (n. 10), early recurrence within 2 months (n. 8) or patient refusal (n. 4). Non-RIOT patients were older (median: 55.4 v 49.3 years, P = .016) and underwent more associated colectomy (45.2 v 25.7%, P = .031). No differences were found concerning ASA score, neoadjuvant therapy, PCI, CC-score, other associated organ resections, pN status or presence of signet ring cells. Overall grades 3–4 morbidity rate was significantly higher in the non-RIOT group (80 v 44.2%, P < .001) with more re-operations (44 *v* 18.6%) or interventional radiology procedures (28.6 v 14.1%). In multivariate analyses, risk factors associated with inability to RIOT were association of surgical and medical complications (OR 12.5, P < .001), isolated medical complications (OR 3.6, P < .001) and PCI (OR 1.1, P = .01). Isolated surgical complications were not (OR 1.1; 95% CI: 0.24–5.06). Non-RIOT patients had shorter overall survival (median OS: 8.3 v 21.2 months, P < .001) and

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disease free survival (P = .01). Among the 47 patients that followed an optimal strategy (CC-0 CRS+neoadjuvant and adjuvant therapies), the 26 who did not present any complication showed a better OS than patients who had some (median OS: 30.7 v 13.1 months, P < .001).

Conclusion

RIOT after HIPEC improves survival in patients with GC. Major postoperative morbidity is the major barrier to RIOT and reduces also its positive impact. Strategies to improve RIOT and to limit morbidity should be investigated.

C120

THE ROLE OF PERITONECTOMY IN CRS PLUS HIPEC

M.C. Hsieh, C.Y. Lu, H.H. Yu, W.W. Chang, P.K. Hsiao, Y.H. Wang

Wan-Fang Hospital Affiliated Taipei Medical University - Taipei (Taiwan, Republic of China)

Objectives

In peritoneal carcinomatosis, cytoreduction surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC) may improve the patient's survival. A complete cytoreduction (cytoreduction score, CS-0/CS-1) is associated with good survival prognosis. To achieve CS-0/CS-1, peritonectomy was frequently performed. However, the peritonectomy procedure is complex and difficult for many surgeons. We evaluate the role of peritonectomy procedure in CRS plus HIPEC.

Methods

We evaluate 344 patients who received HIPEC at our hospital from 2000 till Dec, 2017. Those for prophylactic purpose, laparoscopic HIPEC or repeated HIPEC and already received peritonectomies were excluded. Patients with very high PCI (37–39) were also excluded. Finally, a total of 266 patients were enrolled for this retrospective study. From stepwise analysis according to peritoneal cancer index (PCI), the patients were divided to low PCI (1–6, n = 67), moderate PCI (7–30, n = 166) and high PCI (31–36, n = 33) groups. Patient characteristics, operative procedures, surgical results and oncological results were analyzed. Continues variables were calculated by t-test, and categorized variables were analyzed by chi-square test. Survivals were expressed as Kaplan-Meire methos. P value < 0.05 is considered as significant.

Results

Peritonectomy was associated with a better survival in moderate PCI group, but not in low or high PCI group. It is associated with CS-0/CS-1, prolonged operation time in moderate and high PCI groups, and neoadjuvant chemotherapy in low PCI group. Operative morbidity rates were not increased with peritonectomy in all groups.

Conclusion

Peritonectomy is a part of CRS. In low PCI group, it was easy to achieve CS-0/CS-1 with or without peritonectomy, with subsequent good prognosis. However, in high PCI group, it was difficult to achieve CS-0/CS-1 even peritonectomy were carried out. Performing peritonectomy prolonged the operation time, however, it did not increased morbidity rates. Surgeons should learn to perform peritonectomy procedures in order to achieve a better oncologic outcome by CRS plus HIPEC.

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C121
IMPACT ON THE HEMORRHAGIC COMPLICATIONS OF HIPEC WITH OXALIPLATIN OF THE APPLICATION OF A PROTOCOL OF HIGH DOSAGE OF INTRAVENOUS ALBUMIN

D. Cortes-Guiral[1], I. Lopez-Rojo[2], J. Barambio[2], A. Sanchez[2], I. Prieto[2], I. Guijo-Castellano[2], A. Badia[2], S. Jimenez De Los Galanes[1], H. Guadalajara[2], D. Garcia-Olmo[2]

[1]Hospital Infanta Elena. Peritoneal Oncologic Surgery - Madrid (Spain), [2]Fundación Jiménez Diaz. Peritoneal Oncologic Surgery - Madrid (Spain)

Objectives

Our objective is to describe the impact that the implantation of a protocol of high dosage of intravenous albumin for our patients undergoing cytoreduction and HIPEC, comparing the rates of hemorrhagic complications, specially hemoperitoneum, in our series before and after the systematic application of this protocol.

Methods

62 consecutive patients were analyzed undergoing cytoreduction and HIPEC with maximum dose of intraperitoneal Oxaliplatin (460 mg/m^2), 17 patients did not received high doses of postoperative intravenous albumin and 45 were treated according to the new protocol. This high dose albumin protocol consisted of: intraoperative administration of albumin according to blood test plus one vial of intravenous albumin every 8 hours during the first five postoperative days; if there is hypoalbuminemia, the dose can be increased according to renal function in up to two more vials every 24 hours.

Results

We recorded a decrease in the amount collected by the abdominal drains, with an average decrease in the debit of 280 ml for the first three days. The rate of bone marrow aplasia for the series is of 28% (mild thrombocytopenia). Main hemorrhagic complications in the group of 17 patients out of the protocol were one case of rectus muscle hematoma that required embolization, one acute pericarditis and 2 hemoperitoneum treated with conservative management. In the protocol group, for the 45 patients only one hemoperitoneum were recorded that required surgical treatment and other mild hemoperitoneum (conservative management).

Conclusion

The application of our protocol of high dosage of intravenous albumin has demonstrated a significative decrease in hemorrhagic complications and allows us to use maximum dose of Oxaliplatin with a very low risk of hemoperitoneum. Phase III trial comparing the use of this protocol will be adequate to evaluate the potential of this high dosage of intravenous albumin for our patients undergoing cytoreduction and HIPEC.

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C122
SECOND-LOOK SURGERY AND HIPEC FOR PATIENTS AT HIGH RISK OF PERITONEAL CARCINOMATOSIS OF COLO-RECTAL ORIGIN

I. Lopez-Rojo[1], D. Cortes-Guiral[2], J. Barambio-Buendía[1], A. Leon-Carbonero[3], I. Martin-Valades[3], I. Guijo-Castellano[1], A. Badia[1], I. Prieto[1], S. Jimenes De Los Galanes[2], H. Guadalaraja[1], D. Garcia-Olmo[1]

[1]Peritoneal Oncologic Surgery Department. Fundacion Jiménez Díaz - Madrid (Spain), [2]Peritoneal Oncologic Surgery Department. Hospital Infanta Elena - Madrid (Spain), [3]Medical Oncology. Fundacion Jiménez Díaz - Madrid (Spain)

Objectives

Peritoneal carcinomatosis of colorectal origin can affect up to 30–40% of patients and can be found in up to 10% in the first surgery. Given the low sensitivity of imaging tests and tumor markers to detect early carcinomatosis, Second-look Surgery was developed for patients at high risk of developing carcinomatosis, after receiving adjuvant chemotherapy for their colorectal cancer and with negative radiological tests, before 12 months after the first intervention. It pretends to anticipate clinical and radiological peritoneal involvement. It consists of a laparotomy, cyto-reduction if necessary, with HIPEC. D. Elias published that 56% of high-risk patients, with negative review tests, had carcinomatosis in laparotomy, with this technique it is achieved, a 5-year overall survival of 90% and 5-year disease-free survival of 44%. Our goal is to present the results of our Second-look program for high-risk patients.

Methods

In May 2015, the Second-look protocol for patients at moderate and high risk of developing carcinomatosis was approved in our Hospital: Perforated tumors, peritoneal nodules, ovarian metastases, positive cytology and pT4.

Results

31 patients have been treated according to the Second-look protocol. Seventeen of the patients were found peritoneal disease (55%), all of them completed risk reduction surgery and HIPEC. Four patients presented complications (Dindo Clavien) grade II and another grade IIIa resolved with medical or interventional management. There were no cases of postoperative mortality. No patient has presented peritoneal recurrence.

Conclusion

Carcinomatosis of colorectal origin is predictable, so second look in high risk patients, allows to prevent or detect it, and treat it in its most initial stages with the greatest impact on survival and assumable morbidity and mortality.

C123
IMPACT OF OVARIAN METASTASES ON SURVIVAL IN PATIENTS TREATED WITH CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR PERITONEAL MALIGNANCY OF APPENDICEAL AND COLORECTAL CANCER ORIGIN

A. Mehta, M. Bignell, S. Alves, K. Chandrakumaran, S. Dayal, F. Mohamed, T. Cecil, B. Moran

Peritoneal Malignancy Institute Basingstoke

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Objectives

Ovarian metastases from gastrointestinal tract malignancy have been considered an ominous finding with poor prognosis. The aim of this project was to determine the impact on survival, and potential cure, when cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) are combined to treat peritoneal malignancy in women with Krukenberg tumours.

Methods

Retrospective analysis of prospectively collected data between January 2010 and July 2015. Female patients undergoing complete CRS (macroscopic tumour removal) and HIPEC for pseudomyxoma peritonei (PMP) of appendix origin, or colorectal peritoneal metastases (CPM) were included. Survival was estimated using the Kaplan-Meier method and survival rates compared using the log-rank test.

Results

In total, 889 patients underwent surgery for peritoneal malignancy, of whom 551 were female. Of these, 504/551 (91%) underwent complete CRS and HIPEC. Overall, 405/504 (80%) had at least one involved ovary removed either during CRS and HIPEC or at their index pre-referral operation. 352 patients (87%) had an appendiceal tumour and 53 (13%) had CPM.

At a median follow up of 40 months, overall survival (OS) did not differ significantly between patients with or without ovarian involvement in women with a primary low-grade appendix tumour or CPM. In women with high-grade appendix primary pathology, OS was significantly lower in patients with ovarian metastases compared with those without ovarian involvement.

Conclusion

Women with ovarian metastases from low-grade appendix tumours or colorectal cancer, treated with CRS and HIPEC, have similar survival rates to patients without ovarian metastases. Long-term survival and cure is feasible in patients amenable to complete tumour removal.

Regarding ovarian metastases as a manifestation of peritoneal metastasis can lead to long-term survival and even cure in selected patients treated with CRS and HIPEC. Ovarian metastases should no longer be regarded as ominous and terminal findings in patients with gastro-intestinal malignancy.

C124

TWO-STAGE CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY FOR PSEUDOMYXOMA PERITONEI WITH HIGH PERITONEAL CARCINOMATOSIS INDEX

L. Sidéris, B. Trilling, R. Hamad, P. Dubé, P. Richebe, A. Mitchell

Centre de Recherche du CIUSSS de l'Est-De-L'Ile-De-Montréal, Hôpital Maisonneuve-Rosemont, Université de Montréal, Montréal, Canada - Montréal (Canada)

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Objectives

The accepted standard treatment for pseudomyxoma peritonei (PMP) is complete cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC). High peritoneal carcinomatosis index (PCI) is associated with increased surgical morbidity and mortality. Very high PCI may be considered as a contraindication itself as surgical risk and predictable quality of life would not be acceptable. We hypothesized that PMP patients with very high PCI scores may be treated effectively with a two-stage approach.

Methods

A retrospective review of all PMP patients with a high PCI treated with two-stage CRS followed by HIPEC in our institution was performed. Baseline characteristics, operative details and outcomes were extracted from chart review.

Results

Between July 2001 and July 2017, we identified 116 patients who had been operated for disseminated peritoneal disease originating from the appendix. Eight PMP patients underwent two-stage CRS as a single stage CRS was not possible or was thought to be too invasive due to multiorgan extent. Complete cytoreduction of the inframesocolic compartment was performed during the first stage as to minimize the chance of trauma to the supramesocolic organs during lysis of adhesions. Total colectomy with iliorectal anastomosis, omentectomy and removal of any pelvic or retroperitoneal mass were usually performed. Second stage aimed to perform thorough adhesiolysis of the inframesocolic abdomen, and complete (CCR0) or nearly-complete (CCR1) cytoreduction of the supramesocolic compartment. HIPEC was performed at the end of the second CRS using Oxaliplatin at 460 mg/m^2 for 30 minutes, combined with 5-fluorouracil (5-FU) and folinic acid (LV) intravenous concomitant chemotherapy. There was no mortality. Major complications (Clavien Dindo CD III-V) occurred in 13% of patients following the first stage and 38% following the second stage. The median PCI was 33 at the first stage (IQR 30–39), and 23 at the second stage. Median duration of surgery were 5 and 8 hours for first and second stage, respectively. The median time between surgeries was 4.7 months. Median follow-up was 2.6 years (range:1–9.8). Two patients experienced relapses 8.5 years and 9.5 months after their respective second stage.

Conclusion

This study suggests that a two-stage approach is both feasible and safe for PMP with very high PCI, permitting curative treatment for those patients.

C125

SCLEROSING ENCAPSULATING PERITONITIS SECONDARY TO CYTOREDUCTIVE SURGERY AND HIPEC

G. Liberale[1], M. Pocard[2], S. Mehta[3], W. Ceelen[4], F. Arias[5], O. Glehen[6], P. Sugarbaker[7]

[1]Surgery, Institut J. Bordet (U.L.B.) - Brussels (Belgium), [2]Surgery, Hospital Lariboisière (APHP) - Paris (France), [3]Surgery, Saifee Hospital - Saifee (India), [4]Surgery, Ghent University Hospital - Ghent (Belgium), [5]Surgery, Clinical Care Cancer of Peritoneal Neoplasms - Bogota (Colombia), [6]Surgery, Centre Hospitalier Lyon Sud - Lyon (France), [7]Surgery, Medstar Washington Hospital Center - Washington (United States)

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Objectives

Sclerosing encapsulating peritonitis (SEP) is a rare entity characterized by encapsulation of the small bowel and/or the colon by a fibrous tissue forming a shell. Intraperitoneal (IP) chemotherapy has been reported as a rare cause of SEP and there is only one report of SEP as a potential complication of hyperthermic intraperitoneal chemotherapy (HIPEC) associated to cytoreductive surgery (CRS).

The objective of this study is to review clinical cases of SEP associated to intraperitoneal chemotherapy (IPC).

Methods

Clinical cases of post-HIPEC SEP were collected from PSOGI members. Clinical symptoms, radiologic features, type of intraperitoneal chemotherapy used, and treatment were reviewed.

Results

Data of 13 patients were collected including 9 females and 4 males with a mean age of 55 years. Five patients have been treated by CRS and HIPEC for pseudomyxoma peritonei, 4 for colorectal cancer, 2 for mesothelioma, 1 for appendicular adenocarcinoma and 1 for ovarian cancer. The mean PCI was 11 (1–21). All patients underwent at least a partial peritonectomy. A platine IP drug was used in 9 patients (69%) and MMC with/without doxorubicine in 4 (31%). The most frequent symptom was abdominal pain associated with intestinal obstruction in 10 patients (77%). Interval between HIPEC and symptoms varied from 1 to 32 months. The diagnosis has been made at explorative surgery in 10 patients and suspected on imaging in 5 of them. The majority of patients were treated by lysis of the fibrous sheath surrounding the intestinal bowel after recurrent obstruction episodes.

Conclusion

CRS associated to HIPEC is a potential cause of secondary SEP. However, it remains a rare complication needing in most of the cases a surgical operation to relieve obstructive symptoms.

C126

SELECTION AND CLINICAL CHARACTERISTICS OF EXCEPTIONAL/POOR RESPONDERS IN PERITONEAL DISSEMINATION FROM APPENDICEAL ORIGIN TREATED WITH CRS/HIPEC

C. Munoz-Zuluaga, M.C. King, A. Sardi, P. Ledakis, M. Sittig, C. Nieroda, V. Gushchin

Mercy Medical Center - Baltimore (United States)

Objectives

Predicting response to cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) among patients with peritoneal dissemination (PD) from appendiceal origin (AO) is challenging. We observed patients who responded exceptionally well or very poorly to this standard of care treatment. This study aims to define the complete clinical profile of exceptional and poor responders within histopathologic subtypes.

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Methods

A retrospective review of HIPEC patients with complete cytoreduction (CC-0/1) between 1998–2017 was performed. Histopathology was categorized as DPAM, PMCA, and PMCA with signet ring cells (PMCA-S). Patients were divided into recurrent and non-recurrent groups and median follow up was calculated for each group respectively. Exceptional responders (ER) were defined as alive without recurrence after the median follow-up of the non-recurrent group. Poor responders (PR) were defined by disease recurrence before the median follow-up of the recurrent group. Perioperative characteristics of each histopathology were analyzed.

Results

Overall, 116 DPAM, 83 PMCA, and 51 PMCA-S were identified with median follow-up of 49, 60, and 26 months in the non-recurrent group and 59, 40, and 26 months in the recurrent group, respectively. DPAM, PMCA, and PMCA-S had 47 (41%), 20 (24%), and 7 (14%) ER and 11 (10%), 20 (24%), and 20 (39%) PR, respectively. ER in all subtypes had lower median preoperative peritoneal carcinomatosis index (DPAM: 26 vs 36, $p = 0.005$; PMCA: 11 vs 33.5, $p < 0.001$; PMCA-S: 3 vs 29.5, $p = 0.001$). DPAM and PMCA ER were more likely to have normal tumor markers ($p = 0.003$ & $p = 0.004$), but this was not seen in PMCA-S ER. Negative lymph nodes and lower age were significant characteristics only in PMCA ER ($p = 0.003$ & $p = 0.034$). PMCA and PMCA-S ER were more likely to have CC-0 (no residual disease) than CC-1 (disease < 2.5 mm) ($p = 0.018$ & $p = 0.008$). There was no significant difference between ER vs PR in any subtype for gender, prior surgical score, and time to surgery.

Conclusion

Perioperative characteristics related to ER vs PR are different across histopathologic subtypes in PD from AO treated with CRS/HIPEC. Degree of cytoreduction (CC-0 vs CC-1) differs significantly between ER vs PR in PMCA and PMCA-S, but was not observed in DPAM. This emphasizes the necessity of an aggressive surgical approach with no residual disease for high-grade malignancies. Genetic alteration studies may further elucidate differences between exceptional and poor responders.

C127

MOLECULAR FEATURES OF PATIENTS AFFECTED BY COLON CANCER PERITONEAL CARCINOMATOSIS TREATED WITH CRS AND HIPEC

L. Graziosi, E. Marino, C. Vannoni, A. Donini

University of Perugia - Perugia (Italy)

Objectives

Our study aimed to evaluate the prognostic value of KRAS mutation and the microsatellite stability associated to others clinical and pathological features in colon cancer peritoneal carciomatosis patients.

Methods

This was a single-center prospective study. All 26 patients included underwent cytoreductive surgery and HIPEC for PC from CRC in the Department of General and Emergency Surgery of Perugia from January 2008 to October 2016.

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Data were collected prospectively including patients' demographic data (age and gender), morphological, clinical and pathological data.

Intraoperative PCI, Completeness of cytoreduction, blood loss, blood and plasma units transfused were accurately evaluated.

For each sample, the following histological criteria were sought: the presence of tumor cells, degree of differentiation, TNM classification, the presence of vascular invasion and signet ring cells, the presence of a mucinous component, area of tumor necrosis, immunohistochemical expression of KRAS, and BRAF genotypes, microsatellite sequences stability (MSS) or microsatellite sequences instability (MSI).

Retrospectively, genetic testing was performed on tumor samples taken during HIPEC and stored in our institutional bio bank; it was on the primary tumors if available, and if not on PC or metastases' sample.

Results

26 patients affected by colon cancer peritoneal carcinomatosis were enrolled.

The distribution of the patients according to tumor side was: 8 right colon; 11 left colon, 2 transverse colon; 6 rectum. One patient had a double tumor location.

Median PCI was 3.

CC0 was performed in 92.3% of patients; CC1 in 7,7% of patients.

Mutations of codons 12 or 13 of exon 2 of KRAS status were detected in 38% of patients.

Exone 2 was mutated in 38% of patients; Exone 3 and 4 were Wild Type in all the studied patients.

NRAS was mutated only in one case. BRAF did not show any mutations.

MSI was detected in 15.38% of the tested samples. Of these 75% were low microsatellite instabilities, whereas in 15% there was high microsatellite instability.

5y-OS of all patients was 60% and 5y-DFS was 30%.

According to our results also MSI instability and non-mucinous tumor have a worse prognosis.

Conclusion

To assess the prognosis of colorectal PC patients underwent to CRS and HIPEC procedure, we believe that KRAS status, MisMatch Repair in addition to others pathological features as signet ring cells, mucinous expression are essential.

C128

SURVIVAL ANALYSIS OF PATIENTS TREATED WITH CRS AND HIPEC IN ONTARIO, CANADA

A. Mccart, E. Taylor, M. Nardin, D. Bischof, A. Govindarajan

University of Toronto - Toronto (Canada)

Objectives

Since February 2011, over 250 patients have been treated with cytoreductive surgery (CRS) and HIPEC at our institution. We analyzed the outcomes in the group of patients who have at least 5 years of follow-up data.

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Methods

All patients presenting to our centre who underwent CRS and HIPEC between February 2011 and April 2013 were identified from our prospective database and a retrospective chart review was conducted. Patient demographics, surgical data and post-operative outcomes were examined.

Results

46 patients underwent CRS and HIPEC for colorectal, appendiceal or mesothelioma primaries and were included in the analysis. Median age was 54.5 (16 to 73 y) and 52% of patients were female. An equal proportion of patients had secondary PSM from a colorectal or appendix primary. The median PCI was 15 (1–36). The average OR time was 11.6 h (6–22 h). All but 2 patients had a “curative intent” surgery and a CC0/1 resection. All patients were admitted to the intensive care unit post-operatively. The median stay in the ICU was 3 days (1–14) and the median overall length of stay (LOS) was 15 days (9–51). There were 2 post-operative deaths (4.3%) due to sepsis and a pulmonary embolism. 13% of patients suffered major (> grade 3) complications. 35% of the patients required post-operative TPN. There was one re-operation for a post-operative bleed. 3 patients had long-term issues with bowel function and 3 patients developed incisional hernias. The overall 5 year survival was 0% (0/4) for high grade appendix tumours (e.g. adenocarcinoma ex goblet cell carcinoid), 38% (8/21) for colon carcinomatosis, 75% (3/4) for peritoneal mesothelioma, and 82% (14/17) for LAMN / pseudomyxoma peritonei. The recurrence patterns will be discussed.

Conclusion

A peritoneal surface malignancy program was established in Ontario, Canada in 2011. The morbidity and mortality rates are within the published range and are comparable to similar major cancer surgeries. Although the number of patients per group is small, the 5 year survival rates are generally in keeping with the published data.

C129

LONG-TERM OUTCOMES WITH CYTOREDUCTIVE SURGERY (CRS) AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) IN PERITONEAL CARCINOMATOSIS: 10-YEAR EXPERIENCE FROM A JOINT COMMISSION INTERNATIONAL CERTIFIED CENTER IN A DEVELOPING COUNTRY

F. Arias[1], E. Londoño-Schimmer[2], J. Otero[3], C. Cétares[1], G. Herrera-Almario[1], M. Mora[4], M. Rodriguez[5], S. Rodriguez[5], D. Montaño[5], J.D. Guerra[5], A.F. Cardona[6]

[1]Department of Surgery, Peritoneal Neoplasms Clinical Care Center, Fundación Santa Fe de Bogotá - Bogotá (Colombia), [2]Department of Surgery and Section of Colorectal Surgery, Peritoneal Neoplasms Clinical Care Center, Fundación Santa Fe de Bogotá - Bogotá (Colombia), [3]Clinical Oncology Peritoneal Neoplasms Clinical Care Center, Fundación Santa Fe de Bogotá - Bogotá (Colombia), [4]Peritoneal Neoplasms Clinical Care Center, Fundación Santa Fe de Bogotá - Bogotá (Colombia), [5]Faculty of Medicine, Universidad de los Andes - Bogotá (Colombia), [6]Clinical and Translational Oncology Group, Clínica del Country - Bogotá (Colombia)

Objectives

To report oncological outcomes after cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC) from a center specialized in peritoneal malignancies.

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Methods

A review of 119 CRS/HIPEC patients treated between 2007–2017 at a tertiary referral center in Bogotá, Colombia was performed. Patient characteristics, surgical variables, and postoperative outcomes were prospectively collected and analyzed.

Results

Median age at diagnosis was 51-yo (r, 22–78) and 73% (n = 87) were female. The primary origin of the peritoneal carcinomatosis was the appendix in 64%, advanced ovarian and primary peritoneal serous carcinomas (PC) in 17%, colorectal cancer (CRC) in 10.1%, peritoneal mesothelioma (PM) in 9%, and others in 1.6%. Prior surgical Peritoneal Cancer Index (PCI) was 19 (r, 2–39) and 25.2% were exposed to preoperative chemotherapy. Median time from diagnosis to CRS/HIPEC was 11.4 months (r, 1.0–134.1). Mean operative time was 881 min (SD ± 223 min) and complete cytoreduction rate (CCR) was 81.5% (75% appendiceal tumors, 94% PC, 83% CRC, and 100% PM [p = 0.81]). Grade IV, and V complications according to the Clavien-Dindo classification were reported in 12%, and 4% of patients, respectively. Progression-Free Survival (PFS) was 38.4 months (95%CI 12.6–64.3) and 5-year PFS was 64%. PFS was positively influenced by appendiceal and multicystic mesothelioma histology (p = 0.035) as well as complete cytoreduction (p = 0.0001). At 42-month median follow-up 26 patients have died and the median overall survival (OS) was 108.5 months (95%CI 77.5–139.5). OS of patients with and without relapse was 78.6 months (95% CI 36.1–121.1) and NR (p = 0.002), respectively, and only this variable adversely affected the multivariate analysis (RR 3.7, 95% CI 1.4–9.5; p = 0.007).

Conclusion

CRS/HIPEC is an effective treatment for patients with peritoneal neoplasms providing meaningful long-term survival in low and high-grade tumors and should be considered the standard of care. Our results, from a specialized center in a developing Latin-American country, are comparable to those from first-world centers, implying the importance of group experience in providing high-quality outcomes. Results showed that patients without relapse at the 5th year follow-up marker could be considered cured, but should remain under clinical observation.

C130

THROMBOEMBOLIC EVENTS RELATED TO CYTOREDUCTIVE SURGERY (CRS) AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC)

F. Arias[1], E. Londoño-Schimmer[2], J. Otero[3], C. Cétares[1], G. Herrera-Almario[1], M. Mora[4], M. Rodriguez[5], S. Rodriguez[5], D. Montaño[5], J.D. Guerra[5], A.F. Cardona[6]

[1]Department of Surgery, Peritoneal Neoplasms Clinical Care Center, Fundación Santa Fe de Bogotá - Bogotá (Colombia), [2]Department of Surgery and Section of Colorectal Surgery, Peritoneal Neoplasms Clinical Care Center, Fundación Santa Fe de Bogotá - Bogotá (Colombia), [3]Clinical Oncology Peritoneal Neoplasms Clinical Care Center, Fundación Santa Fe de Bogotá - Bogotá (Colombia), [4]Peritoneal Neoplasms Clinical Care Center, Fundación Santa Fe de Bogotá - Bogotá (Colombia), [5]Faculty of Medicine, Universidad de los Andes - Bogotá (Colombia), [6]Clinical and Translational Oncology Group, Clínica del Country - Bogotá (Colombia)

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Objectives

Identify types and frequency of thromboembolic events and associated morbidity and mortality, as well as the role of inferior vena cava filters (IVCF) in patients undergoing cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC).

Methods

Survival based on primary tumor type and extent of surgery were reported and analyzed for correlations with thrombotic events. Between November 2007 and November 2017, 127 case were performed in a reference center from Colombia. Data on 30-day and 90-day postoperative morbidity and mortality were also analyzed.

Results

Of the 127 cases included, 92 (72.4%) were women and the mean age was 51 years (SD ± 11.3). The primary origin of the PC was the appendix in 65.4%, advanced ovarian and primary peritoneal carcinomas in 14.2%, colorectal cancer in 10.2%, peritoneal mesothelioma in 8.7% and others in 1.6%. Mean preoperative and postoperative peritoneal cancer index (PCI) were 19 (2–39) and 0 (0–8). Completeness of Cytorreduction (CCR) was 0 in 102 cases (80.3%), and 1 in 20 cases (15.7%). 15 patients had grade IV, and 5 grade V complications. Median transoperative bleeding was 1800 ml (200–9000), with 108 patients (85%) requiring transfusional support. Mean operative time was 856 minutes (SD ± 226 min), median length of ICU stay 3 days, in-hospital stay 22 days, and 30-day and 90-day mortality rate were 1.6% and 3.9%, respectively. Thrombosis presented in abdominal splanchnic vessels in 14 patients (11%), pulmonary thrombosis (PT) in 16 (12.6%), and deep vein thrombosis (DVT) in 6 (4.7%). 88% of thrombotic events (30 patients) required therapeutic anticoagulation, whilst 4 had a contraindication. In 88 patients an IVCF was placed in the preoperative period. Relative reduction of the risk of thrombosis due to the use of IVCF was 14% (95%CI 7–24%; p = 0.09). None of the clinical variables impact the risk of thrombosis and this adverse event does not impact mortality from any cause (p = 0.56), progression-free survival (PFS) and overall survival (OS) (p = 0.24 and p = 0.57). There was one death associated to a massive pulmonary embolism.

Conclusion

Thrombosis was a frequent and serious event. It did not impact mortality, PFS, or OS. Compared to other series, we found a higher prevalence of thrombotic events, which could be explained by a more active diagnostic evaluation. We also found that IVCF shows a tendency towards decreasing the risk of thrombosis, and its implementation requires evaluation in prospective studies.

C131

A SYNERGY OF STROMA AND EPITHELIUM CONTRIBUTES TO TUMOUR BIOLOGY AND OVERALL SURVIVAL

N.B. Shannon[1], X.T. Qui[1], D. Ng[1], C.A.J. Ong[1], M.C.C. Teo[2]

[1]National Cancer Center Singapore - Singapore (Singapore), [2]National Cancer Center Singapore - Nbshannon@gmail.com (Singapore)

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Objectives

Molecular profiling of tumour has traditionally assessed tumours as a whole, which comprises a heterogenous population of tumour and stromal cells. Such an approach makes it difficult to assess the contribution that each of these components has on overall tumour biology. We aim to profile these components separately in order to assess whether clinical tumour behaviour may represent a synergy between these two components.

Methods

Laser capture microdissection (LCM) was used to profile epithelium and stroma separately, from 32 samples representing matched normal, primary tumour and peritoneal metastases. Comparing to normal tissue, we generated a signature for tumour epithelium, metastatic epithelium, tumour stroma and metastatic stroma. For each signature, we generated a pathway score and carried out recursive partitioning to highlight components related to tumour prognosis in colorectal cancers from TCGA (COADREAD).

Results

Individual signatures did not reach prognostic significance ($p > 0.05$), including that of metastatic tumour (5-year survival 70 vs 51%, $p = 0.15$). However a combination of components was able to improve prognostic significance (5-year survival 82 vs 40%). The biggest separation was seen for primary tumour and metastatic tumour low (good prognosis), and metastatic tumour high, primary tumour stroma high (poor prognosis). In a multivariable model signature representation, both stroma and metastatic tumour were independently prognostic ($p = 0.038$ and 0.01 respectively).

Conclusion

Tumour biology is driven not just by changes within the tumour cells themselves (normal epithelium, tumour, and metastatic tumour), but also by changes within adjacent stroma and subsequent changes in the tumour-stroma interaction. Both of these components contribute to overall tumour biology and suggest the importance of exploring the tumour-stroma interaction.

C132

THE CUMULATIVE INCIDENCE OF METACHRONOUS PERITONEAL METASTASES OF UICC II/III PT4 COLORECTAL CANCER

P. Schredl[1], A. Dinnewitzer[1], D. Neureiter[2], S. Ciftci[1], J. Holzinger[1], J. Presl[1], K. Emmanuel[1], T. Jäger[1]

[1]Department of Surgery, Paracelsus Medical University - Salzburg (Austria), [2]Institute of Pathology, Paracelsus Medical University - Salzburg (Austria)

Objectives

There is an ongoing debate about the necessity of hyperthermic intraperitoneal chemotherapy procedure in pT4 colorectal cancer patients. It has been demonstrated that these patients have an increased risk of metachronous peritoneal metastases (PM). The aim of this study was to evaluate the cumulative incidence of metachronous PM in UICC II/III pT4 colorectal cancer patients in a tertiary care center.

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Methods

This was a retrospective cohort study of patients undergoing a first resection of a UICC II/III pT4 colorectal cancer in a tertiary hospital between 2003 and 2012. Primary outcome was the cumulative incidence of metachronous peritoneal carcinomatosis (isolated or combined). For cumulative incidence analysis failure was defined as peritoneal metastasis occurrence during the follow-up period. Uni- and multivariate survival analyses were performed using Cox-proportional hazards models.

Results

A total of 191 pT4 colorectal cancer patients (M/F = 95/96) with a median age of 70 years (range 33–98) were identified. Patients with an UICC tumor stage IV (n = 83) and R2 resection status were excluded for further analyses. Of the remaining 96 patients 41 (43%) were classified as UICC stage II and 55 (57%) as UICC stage III. A R0 resection was achieved 90 patients (94%). After following each patient at least for five years an isolated or combined metachronous PM occurred in eleven (12%) and 13 patients (14%) accounting for an overall metachronous PM rate of 25%.

The 3- and 5-year cumulative incidence rates for metachronous PM were 14% (95% confidence interval (CI) 8–26%) and 23% (95% CI 12–40%). The 3-year cumulative incidence rate in R0 resected patients was 13% (95% CI 4–25%) compared to 50% (95% CI 9–99%) in patients with R1 resection. Five-year overall survival rates for patients without, isolated, and combined metachronous PM was 79% (95% CI 65–88%), 10% (95% CI 6–36%), and 31% (95% CI 8–58%) respectively.

Conclusion

With a 5-year cumulative incidence of 23% the occurrence of metachronous peritoneal metastases in UICC II and III pT4 colorectal cancer patients is high. Especially in regard to the disastrous five-year overall survival estimates in this group of patients, the installation of a modified follow-up program is required.

C133
LAPAROSCOPIC GASTRECTOMY ON STAGE 4 GASTRIC CANCER

S.H. Min, Y.S. Cho, Y.S. Park, S.H. Ahn, D.J. Park, H.H. Kim

Seoul National University Bundang Hospital - Seongnam-Si (Korea, Republic of)

Objectives

Laparoscopic gastrectomy has short-term benefits compared to open gastrectomy in advanced gastric cancer patients. In retrospective reviews, survival rate between the two showed no significant difference. There are no studies focusing on the feasibility of laparoscopic gastrectomy on Stage 4 gastric cancer with potentially resectable factors. The objective is to analyze the complication rate and long-term survival rate.

Methods

This is a retrospective review of hospital records from Seoul National University Bundang Hospital. 1483 Advanced gastric cancer patients who underwent laparoscopic gastrectomy from 2003 to 2017 were reviewed and among them, 63 patients were stage 4. Complications rates according to Clavien-Dindo scale were analyzed and 5-year survival rate was calculated with Kaplan Meier analysis.

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Results

Among 63 patients, 36(57.1%) had peritoneal seeding nodules, 13(20.6%) had malignant peritoneal cytology, 5(7.9%) had distant organ metastasis and 12(19%) had distant lymph node metastasis. Within the 36 peritoneal seeding patients, all patients except for five received curative resection for the gastric cancer and total excision or electrocauterization for the seeding nodules. There were five cases of early complication and five cases of long term complications, all below grade 3. 5-year survival rate of stage 4 patients was 25%. When we compared the 5-year survival rate between peritoneal seeding patients with the rest, it was 13.1% vs. 39.4% respectively (P = 0.0136). Two patients (15%) from malignant peritoneal cytology group actually developed peritoneal seeding after surgery and only three patients (8%) from peritoneal seeding group showed peritoneal recurrence after surgery.

Conclusion

Laparoscopic gastrectomy on stage 4 gastric cancer patients seems feasible and adequate according to our long term follow up data. Although the survival rate in peritoneal seeding patients is significantly lower compared to other stage 4 patients, it is still higher than other studies. Also, even though peritoneal recurrence is the most common form of recurrence, only 8% of previous peritoneal seeding patients developed peritoneal recurrence. If the patient is fit for surgery itself, aggressive approach to those with resectable stage 4 factors, might be beneficial.

C134

PERITONEAL SURFACE CALCULATOR (PESUCA): A TOOL TO QUANTIFY THE RESECTED PERITONEAL SURFACE AREA AFTER CYTOREDUCTIVE SURGERY

T. Jäger[1], A. Dinnewitzer[1], P. Schredl[1], D. Neureiter[2], M. Fallaha[3], S. Ciftci[1], T. Kiesslich[4], K. Emmanuel[1]

[1]Department of Surgery, Paracelsus Medical University - Salzburg (Austria), [2]Institute of Pathology, Paracelsus Medical University - Salzburg (Austria), [3]Faculty of Medicine, Imperial College School of Medicine - London (United Kingdom), [4]Institute for Physiology and Pathophysiology, Paracelsus Medical University - Salzburg (Austria)

Objectives

An important and controversial discussed issue during hyperthermic intraperitoneal chemotherapy (HIPEC) is whether the dosimetry of intraperitoneal regimens should be body surface area (BSA) based or concentration based. In most institutions drug dose is calculated based on the body surface area (BSA) in analogy to systemic chemotherapy regimens [mg/m²]. These regimens take BSA as a measure for the effective contact area = peritoneal surface area (PSA) in the Dedrick formula. The aim of our project is to provide an online software solution that is able to quantify the PSA before and after cytoreductive surgery (CRS) in 40 different peritoneal regions.

Methods

Preliminary data of the PSA of 38 consecutive patients undergoing 40 CRS and HIPEC procedures was calculated before and after CRS with a newly developed internet based, proprietary peritoneal surface calculator software (PESUCA, https://pesuca.net [test version]). The peritoneal surface was divided in a supramesocolic visceral/parietal and inframesocolic visceral/parietal peritoneum area consisting of 40 different peritoneal regions. Differences between the groups were estimated with the two sample t-test.

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New data from August 2016 to August 2018 of further 40 HIPEC procedures will be presented at the 11th international workshop on peritoneal surface malignancy 2018 in Paris.

Results

The BSA for the 38 patients (40 procedures) with peritoneal surface malignancies (colorectal n = 18, gastric n = 7, ovarian n = 6, mesothelioma n = 5, and others n = 4) was calculated with the Dubois formula: mean 18,720 cm² ± 1924. Automated calculation of the mean peritoneal surface area (cm²) before CRS revealed 18,590 ± 1917 compared to 13,482 ± 2832 after CRS (P < 0.0001). Supramesocolic visceral peritoneum (3457 ± 356 vs. 2813 ± 537: P < 0.001), Supramesocolic parietal peritoneum (2376 ± 244 vs. 1504 ± 953: P < 0.001), Inframesocolic visceral peritoneum (11,266 ± 1162 vs. 8540 ± 1915: P < 0.001), Inframesocolic parietal peritoneum (1491 ± 154 vs. 626 ± 520: P < 0.0001).

Conclusion

For the first time, to the best of our knowledge, it is now possible to approximately calculate and quantify the resected PSA in patients after cytoreductive surgery. Our software provides the possibility to quantify the imperfect correlation between actual PSA and calculated BSA of patients undergoing cytoreductive surgery. We want to stimulate a discussion regarding the dose adjustment of intraperitoneal chemotherapy during HIPEC based on the calculated PSA after cytoreductive surgery.

C135

RAS MUTATION CONFERS PROGNOSTIC SIGNIFICANCE IN PATIENTS UNDERGOING CRS-HIPEC FOR COLORECTAL CANCER

C. Clarke, Z. Morgan, M. Hembrook, S. Tsai, K. Christians, H. Mogal, T.C. Gamblin

Medical College of Wisconsin - 5/1/2018 (United States)

Objectives

Approximately 5% of patients with colorectal cancer (CRC) will present with peritoneal carcinomatosis (PC) with a mean overall survival (OS) of 6-months if left untreated. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is a complex surgical approach used to treat peritoneal carcinomatosis (PC) and the role of this procedure in CRC continues to evolve. There remains a significant need to further identify prognostic factors to facilitate better risk stratification for CRS-HIPEC patients. We performed a single institution study of CRC patients undergoing CRS-HIPEC with curative intent to identify if known genomic drivers of CRC are associated with recurrence-free or overall survival in this patient population.

Methods

Patients with CRC evaluated for CRS-HIPEC at the Regional Therapies Program at the Medical College of Wisconsin from 2010–2017 were identified. Patients with non-CRC pathology, progression of disease precluding surgical intervention and/or HIPEC for palliation were excluded. Patients who had CRS only or did not receive at least 60 minutes of HIPEC were excluded. Clinicopathologic data including age, sex, PCI score, completeness of cytoreduction, lymphovascular invasion, neutrophil-lymphocyte ratio, histology, microsatellite stability, BRAF and RAS mutation status were collected and analyzed.

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Results

47 patients underwent CRS- HIPEC with curative intent. Median PCI score was 14 [IQR: 6–21]. 34 (72%) patients had complete (CC0) resection, 11(23%) had CC1 (≤0.25 cm residual tumor) resection, 2 (4%) had CC2 (0.25–2.5 cm) resection. 6 (13%) of CRC were MSI-high. 22 (47%) were RAS mutant, 4 (9%) BRAF mutant. At median follow-up of 2 years, 23 (48%) died of disease with a median overall survival (OS) of 19 months [IQR: 10–27], 36 (77%) patients developed recurrence with a median disease free survival (DFS) of 7 months [IQR: 5–12]. No factors analyzed reached significance for OS. RAS mutation status and LVI were the only significant predictors of decreased DFS (p = 0.02 and 0.03 respectively) on univariate analysis. On multivariate analysis neither remained significant.

Conclusion

CRS HIPEC can achieve improved survival in patient with PC from CRC, however better risk stratification is needed for patient selection. RAS mutation status is an independent marker of poor prognosis and may provide enhanced prognostic information in these high risk patients. Larger cohort studies are needed to validate these findings.

C136

THE RISK OF PERITONEAL METASTASES IN PATIENTS WITH PT4A VERSUS PT4B COLON CANCER

V.P. Bastiaenen[1], C.E.L. Klaver[1], K.A.T.G.M. Wasmann[1], I.D. Nagtegaal[2], B. Van Ramshorst[3], A.M. Wolthuis[4], J.D.W. Van Der Bilt[1], H.C. Van Santvoort[3], J.H.W. De Wilt[5], A.D. D' Hoore[4], P.J. Tanis[1]

[1]Department of Surgery, Academic Medical Center - Amsterdam (Netherlands), [2]Department of Pathology, Radboud University Medical Center - Nijmegen (Netherlands), [3]Department of Surgery, St. Antonius Hospital - Nieuwegein (Netherlands), [4]Department of Abdominal Surgery, University Hospital Leuven - Leuven (Belgium), [5]Department of Surgery, Radboud University Medical Center - Nijmegen (Netherlands)

Objectives

Patients who underwent curative resection of pT4 primary colon cancer are at high risk of developing peritoneal metastases (PM). With the evolving treatment strategies aiming at prevention or early detection of PM, identification of high-risk patients becomes increasingly important. The primary aim of this study was to determine the risk of PM for the pT4a and pT4b subgroups separately. The secondary aim was to investigate whether the location of ingrowth of pT4b tumours influences the risk of PM, since it is hypothesized that pT4b tumours with ingrowth in intraperitoneal organs carry a higher risk at PM than pT4b tumours with sub- or retroperitoneal ingrowth.

Methods

All consecutive patients from four centres who underwent curative intent treatment for pT4N0-2M0 primary colon cancer between January 2000 and December 2014 were included. Patients were subclassified into those with pT4a and pT4b stage disease. The patients with pT4b tumours were further subdivided into two groups based on the location of ingrowth of the tumour. Primary outcome was the 5-year PM rate assessed using Kaplan-Meier analysis. Secondary endpoints were 5-year other recurrence rate, 5-year disease free survival (DFS) and 5-year overall survival (OS).

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Results

In total, 294 patients with a pT4a tumour and 123 patients with a pT4b tumour were included. During a median follow-up of 50 months (IQR 25–60), 85 patients (20.4%) developed PM. Median time to diagnosis of PM was 14 months (IQR 7–24.5) and 93% of the PM were detected within 3 years. The 5-year PM rate was 26% and 19% for pT4a patients and pT4b patients, respectively (p = 0.263). Other recurrence within 5 years after primary surgery was reported in 40.5% of pT4a patients versus 42% of pT4b patients (p = 0.995). 5-year DFS and 5-year OS were 45.5% and 39.1% (p = 0.267) and 63.7% and 55.7% (p = 0.256) for pT4a and pT4b patients, respectively. Subgroup analyses of the pT4b patients will follow.

Conclusion

No differences regarding risk of PM, other recurrence and survival were found between pT4a and pT4b colon cancer patients. Within the pT4b subgroup, the risk of PM potentially depends on the location of ingrowth (intraperitoneal versus sub-/retroperitoneal), which is currently investigated by our research group.

C137

CURRENT MORBIDITY AND MORTALITY OUTCOMES OF CYTOREDUCTIVE SURGERY WITH HEATED INTRAPERITONEAL CHEMOTHERAPY

M. Peyroteo, A. Cruz, A.R. Monteiro, P. Carvalho Martins, R. Canotilho, A. Sousa, F. Senra, D. Brito, F. Sousa, M. Fernandes, F. Faria, A. De Sousa

IPO Porto - Porto (Portugal)

Objectives

Cytoreductive surgery (CRS) with heated intraperitoneal chemotherapy (HIPEC) is a well-established treatment option for selected patients with peritoneal carcinomatosis. Historically, it has been linked to high morbidity rates and with the routine admission of patients in an intensive care unit (ICU) for postoperative surveillance. However, with the creation of specialized centers, these assumptions have been questioned. Our aim was to evaluate the morbidity and mortality outcomes and the need for routine ICU admission.

Methods

Single center review of patients submitted to CRS and HIPEC between January 2016 and December 2017. At our center all patients are admitted to an intermediate care unit and only selected patients are admitted in the ICU for postoperative surveillance.

Results

104 surgeries were performed in this period of time on 102 patients. The median age was 58 years old and 72.1% of the patients were female. The overall 60-day morbidity rate was 32.8% (n = 34) with 8.7% (n = 9) of major complications (CTCAE 3–4) and 1% (n = 1) death (CTCAE 5). In univariate analysis the number of visceral resections, blood loss during surgery, duration of surgery and peritoneal carcinomatosis index (PCI) were statistically significant factors for postoperative morbidity. In multivariate analysis, duration of surgery had the highest odds ratio (OR 1.21) for postoperative morbidity. 27.9% (n = 29) of patients were admitted in the ICU for postoperative surveillance (≤48 h). The cohort admitted to the intermediate care unit demonstrated similar overall morbidity rate (36% vs. 24%; p = 0.248) than the patients admitted to the ICU for ≤48 h.

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Conclusion

CRS with HIPEC is a safe treatment when done in specialized centers on selected patients. Routine admission to the ICU doesn't seem to be necessary, which supports the current practice at our center of selective admission. This practice proves to be safe with potential implications on cost reduction.

C138

CONTINUOUS EVOLUTION IN COMPLEX SURGICAL PROCEDURES: LESSONS LEARNED FROM A PERITONEAL SURFACE MALIGNANCY CENTER

A. Ben-Yaacov[1], Y. Dux[1], A. Bilik[1], M. Adilah[1], G. Shtrechman[1], D. Aderka[1], E. Shacham-Shmueli[1], A. Hubert[2], A. Beny[3], D. Hazzan[1], D. Zippel[1], A. Nissan[1]

[1]Tel-Aviv University, Sorasky Medical School - Tel-Aviv (Israel), [2]Hadasha Medical Center - Jerusalem (Israel), [3]Rambam Medical Center - Haifa (Israel)

Objectives

BACKGROUND: Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) is a complex surgical procedure widely used for the treatment of peritoneal surface malignancies. The ability to perform such complex surgical procedures safely and effectively depends on both personal and institutional learning curves. The aim of the present study was to better understand the improvement process in CRS/HIPEC over a decade of experience.

Methods

METHODS: This is a retrospective analysis of a prospectively maintained CRS/HIPEC database. A total number of 375 patients with peritoneal surface malignancies (PSM) were treated between 2007 and 2018. CRS/HIPEC was completed in 292 patients (77.8%). Patients with incomplete datasets (n = 23) were excluded from the analysis. The cohort was divided into 4 time periods: Group 1 (2007–2009, n = 29), group 2 (2010–2012, n = 31), group 3 (2013–2015, n = 101), group 4 (2016–2018, n = 108). Patients were analyzed for the following outcomes: operative time, estimated blood loss, number of packed cells transfused, ICU stay, hospital stay, post-operative complications and mortality (Clavien-Dindo classification). Each parameter was analyzed for each group (categorical) by Chi-square or as a continuous variable or by ANOVA test.

Results

RESULTS: Hospital stay and ICU stay were (group 1: 26.5, 4.8 days; Group 2: 31.5, 7.33; Group 3: 16.1, 2.4; Group 4: 19.9, 1.7, p = 0.017, p = 000.1, respectively). Continuous improvement was measured in the mean operative time (8.5, 6.0, 4.9, 5.2 hours), mean estimated blood loss (752, 479, 415, 521 ml) and number of packed cells (2.5, 1.6, 1.1, 0.9 units) for groups 1–4, respectively, p = 000.1. Grade 3–4 complications were 27.6%, 35.3%, 20.8% and 17.6% respectively, while mortality was 3.4%, 8.8%, 3.1% and 4% for groups 1–4 respectively.

Conclusion

CONCLUSIONS: CRC/HIPEC is a complex procedure with a long learning curve. There was improvement with time in all parameters measured. However, improvement was not linear with a pick of major morbidity and mortality and as a result, longer ICU and hospital stay in second phase of the learning curve.

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C139
RETROSPECTIVE ANALYSIS OF ADJUVANT SYSTEMIC CHEMOTHERAPY IN PATIENTS WITH PERITONEAL METASTASIS OF COLORECTAL CANCER TREATED WITH CRS+HIPEC

E.C.E. Wassenaar[1], K.P. Rovers[2], R.J. Lurvink[2], F.J.H. Hoogwater[3], nS.W. Nienhuijs[2], M.J. Wiezer[1], I.J.H.T. De Hingh[2], D. Boerma[1]

[1]St. Antonius Hospital - Nieuwegein (Netherlands), [2]Catharina Hospital - Eindhoven (Netherlands), [3]University Medical Center - Groningen (Netherlands)

Objectives

There is no consensus on administering perioperative systemic chemotherapy (CT) in patients with peritoneal metastasis of colorectal cancer (PM-CRC). The aim of this retrospective study is to investigate the role of adjuvant systemic chemotherapy in patients with PM-CRC treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS+HIPEC).

Methods

The characteristics of patients with pathologically proven PM-CRC treated with CRS+HIPEC between 2005–2017 in two tertiary referral centers were analyzed. The administration of adjuvant systemic chemotherapy varied among centers and in time. Patients receiving ≥2 cycles of adjuvant chemotherapy were placed in the adjuvant CT-group. Primary outcome was overall survival (OS) and secondary outcome parameters were disease free survival (DFS) and completion of chemotherapy regimens after CRS+HIPEC.

Results

In this study, 468 patients with PM-CRC treated with CRS+HIPEC were included. After excluding 22 (4,7%) patients with treatment related death, and 22 (4,7%) patients with unknown status of chemotherapy treatment, 424 patients were included in the analysis. The median OS in the adjuvant CT-group was 36,7 months (n = 198, IQR 23,1–63.0) versus 16,2 months (n = 226, IQR 5,0–14,3), $p < 0,001$ in the non-CT group. The median DFS was 19,1 months (IQR 11,3–35,3) versus 8,4 months (IQR 5,0–14,3) $p < 0,001$. In the adjuvant CT-group, 75% received CAPOX regimen, 18% capecitabine monotherapy, 5% FOLFOX and 1% FOLFIRI. 104 (53%) patients completed their planned CT regimen with or without dose reduction. 50 patients (25%) switched CT regimen and finished the second CT regimen. 38 (19%) patients discontinued CT treatment because of toxicity or disease progression.

Conclusion

This retrospective study shows an overall survival benefit of adjuvant systemic chemotherapy in patients with PM-CRC treated with CRS+HIPEC. The results underline the importance of prospectively assessing the added value of adjuvant systemic chemotherapy in a randomized controlled setting.

C140
PRIMARY TUMOR LOCATION PREDICTS COLORECTAL CARCINOMATOSIS BURDEN IN PATIENTS UNDERGOING CYTOREDUCTIVE SURGERY DESPITE KRAS OR LVI STATUS

K. Lafaro, O. Eng, A. Blakely, M. Raoof, B. Lee

City of Hope National Medical Center - Duarte (United States)

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Objectives

Primary tumor location and tumor characteristics such as KRAS mutation are prognostic for metastatic colorectal cancer and predict response to first-line chemotherapy. However it is not known if primary tumor location is independently associated with the burden of disease at the time of cytoreductive surgery(CRS) or completeness of cytoreduction(CCR) in patients with peritoneal carcinomatosis(PM).

Methods

A retrospective review of a prospectively maintained institutional database of patients undergoing CRS±heated intraperitoneal chemotherapy(HIPEC) from 1/2009–8/2016 was performed to examine demographics, primary tumor characteristics, presence of lymphovascular invasion(LVI), KRAS mutation status, MSI status, peritoneal carcinomatosis index(PCI) and CCR in patients who underwent CRS/HIPEC for colorectal adenocarcinoma. MSI status was excluded due to lack of MSI high tumors. Cut-off for right sided tumors was proximal to the splenic flexure. Analysis of covariance was performed to determine independent predictors of PCI.

Results

Fifty-five patients underwent CRS±HIPEC for colorectal cancer with PM. A majority were left-sided primary tumors (n = 30,54.5%). Median age was 53 and majority of patients were female (28,50.9%). Median PCI was 9(2–31). KRAS mutation status was available for 42 of which 24 had mutations (57.1%). On univariate analysis there was no difference in demographics or tumor characteristics between right and left-sided tumors. Patients with a known KRAS mutated tumors had similar median PCI as KRAS wildtype (11.167[95% CI 8.05–14.28] vs. 10.111[95% CI 6.32–13.9], p = 0.654). However, patients who underwent CRS/HIPEC for right sided primary had a higher median PCI than left sided (14.80[95% CI 9.90–19.70] vs. 8.625[95%CI 6.5–10.73], p = 0.008). This persisted after adjusting for patient demographic and tumor characteristics including KRAS status and LVI (F-statistic 5.266, p-value = 0.020). Patients with right-sided tumors were more likely to have incomplete cytoreduction (CCR2/3) compared to those with the left sided tumors(20% vs. 0%, p = 0.01). All patients who had CCR2/3 had KRAS mutant tumors.

Conclusion

Primary tumor location is independently correlated with the burden of carcinomatosis at the time of CRS and is associated with the ability to achieve complete cytoreduction even taking into consideration KRAS mutation status and LVI. While KRAS mutation was not associated with higher PCI, it does seem to affect CCR and thus may ultimately impact survival in future studies.

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CLINICAL OUTCOMES OF PATIENTS WITH EXTENSIVE PERITONEAL CARCINOMATOSIS OF COLORECTAL OR APPENDICEAL ORIGIN UNDERGOING CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY

N.L. De Boer[1], K. Rovers[2], E.V. Madsen[1], A.R. Brandt[1], C. Verhoef[1], I.H. De Hingh[2], J.W. Burger[1]

[1]Department of Surgical Oncology, Erasmus MC Cancer Institute - Rotterdam (Netherlands), [2]Department of Surgical Oncology, Catharina Hospital - Eindhoven (Netherlands)

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Objectives

Cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) is standard of care for patients with peritoneal carcinomatosis (PC) of colorectal or appendiceal carcinoma and a low/moderate disease load. The abdominal disease load is evaluated by the peritoneal cancer index (PCI). General consensus is, that in case of a PCI above 20, CRS-HIPEC is not beneficial. In the last 11 years we have collected a small group of patients with a PCI > 20 that, after being discussed in a multidisciplinary team, did undergo CRS-HIPEC. Aim of this study is to explore the clinical outcomes of this selected patient group.

Methods

A retrospective observational study was conducted in two hospitals in the Netherlands; the Erasmus MC Cancer Institute in Rotterdam and the Catharina Hospital in Eindhoven. All patients with extensive PC from colorectal of appendiceal cancer that underwent CRS and HIPEC between July 2007 and March 2018 were included. Extensive PC was defined as patients with a PCI of 20 or more. Patient characteristics and the peri- and postoperative course (including hospitalization, post-operative morbidity, mortality and survival) were reviewed.

Results

A total of 31 patients were included in the study. The majority of patients had a peritoneal carcinomatosis of colorectal origin (83.9%), and 16.1% was of appendiceal origin. Median PCI-score was 22 (IQR 21–23). All patients underwent open CRS-HIPEC procedure. Most patients, 87.1%, underwent complete cytoreduction (R1-resection), 12.5% had a R2a-resection (residual tumor < 2.5 mm). Severe post-operative morbidity (grade 3–4) occurred in 48,2% of patients. In hospital mortality was 0%. The median overall survival (OS) was 22 months (95% confidence interval 14,5–29,5). OS at 1 and 2 years was 70.7%, 28.3%, respectively. There was no statistical significant difference in OS between patients with colorectal or appendiceal carcinoma.

Conclusion

Our study shows that CRS and HIPEC is feasible in selected patients with high PCI. We think high PCI alone should not be a contraindication for CRS and HIPEC. However, institutional experience and adequate patient selection is essential to reduce the chance of postoperative complications in this specific population.

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BLOOD TRANSFUSION IS ASSOCIATED WITH POOR SURVIVAL IN PATIENT TREATED WITH CRS AND HIPEC FOR PERITONEAL METASTASIS

G. Mariano, E. Gayat, R. Schiavone, S. Dagois, M. Pocard, C. Eveno

Lariboisiere Hospital - Paris (France)

Objectives

The combination of cytoreductive surgery (CRS) and hyperthermic intra-peritoneal chemotherapy (HIPEC) is characterized by a high rate of major morbidity, especially with hemorrhagic complication. The need of blood transfusion (BT) after primary cancer surgery may influence long term survival. The need for blood transfusion could be decrease and controlled: using preoperative iron intravenous infusion in case of planed surgery and using HIPEC drugs not associated with an increased risk as. We aimed to evaluate the predictive factor of operative and postoperative blood transfusion and its influence on disease free (DFS) and overall survival (OS) after CRS and HIPEC.

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Methods

A post-hoc analysis of a prospective cohort of 645 patients with peritoneal carcinomatosis (PC) from 2006 to 2016 was undertaken. Demographic variable, PC origin and characteristics of surgery were analyzed as well as the influence of the blood transfusion on postoperative complications (POC), progression free (PFS)and overall survivals (OS) and hospital length of stay (LOS).

Results

CRS and HIPEC was performed in 471 (73%) patients, including the use of oxaliplatin in 87% patients. Two hundred three patients (32%) received a BT, representing the BT group. More complete resection and digestive anastomosis were performed in the BT group (87% vs. 77%, $p < 0.05$ and 57% vs. 40%, $p < 0.001$, respectively). Rate of CRS+HIPEC was higher in the BT group (82% vs. 69%, $p < 0.001$) including more oxaliplatin-based HIPEC (75% vs. 59%, $p < 0.001$). Major morbidity was higher in case of BT, with 15% in non BT group and 48% in the BT group ($p < 0.0001$); including higher hemorrhagic complication (2% vs. 27%, $p < 0.0001$) and reoperation (9% vs. 42%, $p < 0.0001$) rate. Pre-operative mean hemoglobin (Hb) was lower in the BT group 12.4 (11 to 13.3) vs. 13.3 g/dL (12.3 to 14.2) ($p < 0.0001$). LOS was increased in the BT group 12 (9 to 16) vs. 19 days (13 to 32.5) ($p < 0.0001$). OS and DFS were comparable between the two groups (HR and 95% CI at 1.16 [0.64–2.11] and 1.29 [0.98–1.71], respectively). In sub-group analysis, patients with compete CRS had worst OS and DFS when they received blood transfusion.

Conclusion

BT is associated with extensive surgery and the use of oxaliplatin, leading to high a rate of major morbidity. Its effect on DFS and OS in patients with complete CRS is of major impact. As low preoperative Hb is associated BT, corrective factor could be implemented to improve early and long term outcomes.

C143

SURGERY CHARACTERISTICS AND TREATMENT OF HEMORRHAGIC COMPLICATION AFTER CYTOREDUCTIVE SURGERY HYPERTHERMIC INTRA PERITONEAL CHEMOTHERAPY: A RETROSPECTIVE COHORT STUDY OF 67 PATIENTS

H. Courcier, G. Mariano, E. Gayat, M. Ledorze, M. Pocard, C. Eveno

Lariboisiere Hospital - Paris (France)

Objectives

Cytoreductive surgery and Hyperthermic Intra Peritoneal Chemotherapy (CRS+HIPEC) is the treatment of choice of peritoneal carcinomatosis (PC). This procedure is known to generate high major morbidity rate with increased risk of postoperative hemorrhagic complications (HCs). The aim of this study was to analyze the risk factors of HCs and the different modalities of treatment.

Methods

Five hundred and twenty one patients who had CRS+HIPEC between 2006 and 2016 were included. Sixty-seven patients (13%) experienced HCs. Demographic variable, carcinomatosis origin, characteristics of surgery and post-operative complication were analyzed as well as the analyze of the therapeutic strategy when HCs occurred.

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Results

The study population was 57 years old patients, 73% female, ASA score of II (61%), 72% received preoperative chemotherapy, with a pre-operative rate of hemoglobin of 12,8g/dl±1,6. Primitive cancers were colorectal (52%), peritoneal pseudomyxoma (16%) and ovarian (12%) cancer. During surgery, mean peritoneal carcinomatosis index (PCI) was 11, mean number of removed organs was 4. 58% of the patients had digestive anastomosis, 30% and 36% had Douglas pouch and diaphragm peritonectomy. Oxaliplatin was used for 98,5% of the HIPEC. Total blood loss during surgery was 295 mL ± 288 mL and length of surgery was 495 min ± 125 min. 67% of the patients were diagnosed with HCs during the 5 postoperative days, with a hemodynamic instability and blood in the suction tube in 24% and 57% of the cases. 86,5% of patients had a blood transfusion for HC. At the diagnosis of HCs, 76% and 55% of the patients had hemoglobin rate <9 g/dL and platelets count was <150 × 109/L. An abdominal CT scan was performed in 60% of the patients. Active bleeding was diagnosed in 30% and an hematoma in 87,5%. 79% had a surgical treatment including 92% during the first 24 hours with a success rate of 70%. Conservative attitude was decided for 21% of the patients, successful in 43%. On a total of 61 patients reoperated for HCs, 12(19,6%) were operated twice and 3(4,9%) were operated three times. Major morbidity rate was 94% including 5 patients (7,5%) who died in the HCs group.

Conclusion

Hemorrhagic complication after CRS with HIPC is severe, leading to high a rate of mortality. It occurs most frequently in the 5 days following the surgery. The surgical treatment is mainly mandatory and sometimes needs to be repeated. Predictive factors of surgery success for optimal treatment of HCs have to be analyzed.

C144

THE ROLE OF PERIOPERATIVE CHEMOTHERAPY FOR PERITONEAL METASTASES OF COLORECTAL CANCER ORIGIN TREATED WITH CURATIVE INTENT

G. Liberale[1], D. Repullo[1], S. Barbois[2], D. Leonard[2], A. Bohlok[1], E. Thys Van Den Audenaeren[2], A. Hendlisz[3], M. Van Den Eynde[4], A. Kartheuser[2]

[1]Surgical oncology, Institut J. Bordet - Brussels (Belgium), [2]Unité de Chirurgie Colorectale, Clinique Universitaire St Luc - Brussels (Belgium), [3]Medical Oncology, Institut J. Bordet - Brussels (Belgium), [4]Medical Oncology, Clinique Universitaire St Luc - Brussels (Belgium)

Objectives

Cytoreductive surgery (CS) plus hyperthermic intraperitoneal chemotherapy (HIPEC) is the standard treatment for peritoneal metastases (PM) of colorectal origin, providing overall survival (OS) of 19% to 39% at 5 years. However, the role of perioperative chemotherapy (PCh) in this setting remains controversial.

The aim of this study was to compare disease-free survival (DFS) and OS of patients treated with CS and HIPEC with or without perioperative chemotherapy (PCh).

Methods

We performed a retrospective bicentric study including patients treated with complete CS (R1) and HIPEC for initially resectable PC of colorectal origin. Patients with hepatic metastasis (HM) were included as long as they had less than 3 metastases and were candidates for resection (R0) before or during CS. Both groups were analyzed and compared for sex, age, lymph node staging, PCI score, tumor differentiation, tumor location, and presence of HM.

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Results

One hundred twenty-five patients treated between 2008 and 2017 were included. Seventy-four patients did not receive any PCh and 51 received PCh. Both groups were well balanced for all factors. The median follow up was 26 months for both groups. Median survival was 41 months for the PCh group and 69 months for the no treatment group (p = 0.073). One-year OS and DFS were 91.6% and 48.7%, respectively, for the PCh group and 95.7% and 55.5%, respectively, for the no treatment group. Three-year OS and DFS were 52.4% and 12.5%, respectively, for the PCh group and 68.8% and 26.9%, respectively, for the no treatment group.

Conclusion

These preliminary results suggest that PCh does not provide additional benefit to patients treated by CS and HIPEC for PM of colorectal cancer origin.

C145

SURGERY AND EMPATHY: TWO SIDES OF AN OPTIMIZED TREATMENT OF PATIENTS WITH PERITONEAL DISEASES

L. Robieux[1], F. Zenasni[2], C. Flahault[1], M. Pocard[3], C. Eveno[3]

[1]Université Paris Descartes, Laboratoire Psychopathologie et Processus de Santé - Paris (France), [2]Université Paris Descartes, Laboratoire Adaptations Travail Individu - Paris (France), [3]Lariboisiere Hospital - Paris (France)

Objectives

Empirical data in psycho-oncological studies show the necessity to consider the doctor-patient communication and its positive impact on outcomes such as patients' satisfaction, treatment adherence, physical and psychological wellbeing. In this line, the present research aims to define the role and determinants of an effective doctor–patient communication during the treatment of patients with peritoneal carcinomatosis (PC).

Methods

We carried out a prospective longitudinal study including patients treated for peritoneal carcinomatosis of various origins. From November 2016, to date, data were collected using validated questionnaires at two times of evaluation: one month before the surgery (T0) and one month after (T1). Thus, patients reported their (a) anxiety and depression levels, (b) standardized and individualized quality of life and (c) how they perceived communication, attitude and empathy of the surgeon.

Results

105 volunteer patients (Mean age = 58.18 years, SD = 10.24, 62.2% female) participated to the study. PC arose from rare diseases (14%), colorectal (38%), eso-gastric (24%) and ovarian (8%) cancer. Three groups are defined according to the severity of their pathology and the treatment offered to them: (1) Cytoreductive surgery and Hyperthermic Intra Peritoneal Chemotherapy (CRS+HIPEC, 53%), (2) Pressurized Intra Peritoneal Aerosol Chemotherapy (PIPAC, 17%), and (3) the patients recused for surgical treatment, treated with exclusive intra venous chemotherapy (30%). Results are presented according to Baron and Kenny recommendations. The regressions analyses show that only depression and anxiety are sensitive to the communication and empathy of surgeon. The main results show that a good communication and high level of

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empathy at T0 and T1 limit depression and anxiety of the patients in T1 ($Test\ t_{depression} = -1{,}64\ ;\ ddl = 25\ ;\ p < .05\ ;\ Test\ t_{anxiety} = -1{,}27\ ;\ ddl = 25\ ;\ p < .05$). Results also indicate that the severity of the disease modulates this positive impact of communication: better is the communication the less are the level of depression and anxiety of the patients. This effect is higher for patients treated for the more severe disease ($F(1,23) = 4.13$; $p < .05$).

Conclusion

These results confirm that, even in the case severe disease a good communication between patient and physician remains a significant factor in promoting the well-being of patients.

C146

CYTOREDUCTION AND HIPEC IN THE TREATMENT OF COLORECTAL PERITONEAL METASTASIS. MORBIDITY, MORTALITY AND SURVIVAL

V. Concepcion Martin, C. Diaz, R. Gianchandani, J.M. Sanchez, C. Chocarro, E. Moneva, M. Barrera

Hospital Universitario Nuestra Señora de Candelaria - Santa Cruz de Tenerife (Spain)

Objectives

Our aim is to expose the results of our center in the treatment of peritoneal disease from colorectal origin using CCR and HIPEC.

Methods

We analyze the data from our prospective database from January 2011 to December 2017, including morbidity, mortality and survival to date.

Results

We performed 146 HIPEC procedures, 53 of them with disease from colorectal origin. We performed a second procedure in three patients, and three in another of our patients.

We have 25 men and 22 women in our series, with a median of 57 years old. We achieved a CC0 resection in all cases. Median Peritoneal Carcinomatosis Index was 7 (0–24). A median of two peritonectomies was necessary, with 78% visceral resections. A derivative stoma was considered necessary only in 6 cases. 37 patients required some type of intestinal anastomosis, and we had three colorectal anastomosis leaks (8%). Only 30% of the cases required transfusion during surgery. The mean postoperative stay was 14 days.

Mortality in our series was 2%, because of cardiac complications after surgery. Over all morbidity was 45%, with major complications (Clavien-Dindo > IIIb) in 11 patients (20%).

From the 47 patients of our series we have one patient lost in the follow-up. With a mean follow-up of 33 months, 73% patients are alive. Seven patients have a disease free survival of more than 36 months.

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Conclusion

In the last years, cytoreductive surgery and HIPEC has proved his efficacy in the treatment of peritoneal metastasis, and it can improve the survival of patients treated until now with endless cycles of chemotherapy. Our results are similar to those published in the literature. We believe that oncologic surgeons and medical oncologists can combine forces to provide the best possible treatment, and that treatment includes cytoreduction and HIPEC.

C147

SELECTION OF THE OPTIMAL CHEMOTHERAPY REGIMEN FOR HIPEC IN GASTRIC CANCER WITH PERITONEAL METASTASIS- FRENCH MULTICENTER ANALYSIS FOR THE BIG-RENAPE GROUP

K. Polom[1], P.E. Bonnot[2], E. Decullier[3], L. Villeneuve[4], M. Pocard[5], F. Quenet[6], J.M. Bereder[7], P. Meeus[8], K. Abboud[9], S. Msika[10], P. Rat[11], C. Arvieux[12], T. Courvoisier[13], A. Lefevre[14], D. Pezet[15], N. Pirro[16], R. Wernert[17], R. Kianmanesh[18], D. Goere[19], O. Glehen[2]

[1]Department of Surgical Oncology, Medical University of Gdansk - Gdansk (Poland), [2]Hospices Civils de Lyon, Centre Hospitalier Lyon-Sud, Surgical Oncology - Lyon (France), [3]Hospices Civils de Lyon, Unité de Recherche Clinique,Pôle IMER - Lyon (France), [4]Hospices Civils de Lyon, Unité de Recherche Clinique,Pôle IMER - Lyon (France), [5]AP-HP, Hôpital Lariboisière, Surgical Oncology - Paris (France), [6]Institut du Cancer de Montpellier,Surgical Oncology - Montpellier (France), [7]CHU Nice,Digestive and Visceral Surgery Department - Nice (France), [8]Centre Léon Bérard, Surgical Oncology - Lyon (France), [9]CHU Saint Etienne,Digestive and Visceral Surgery Department - Paris (France), [10]AP-HP, CH Louis Mourier, Digestive and Visceral Surgery Department - Paris (France), [11]CHU Dijon,Digestive and Visceral Surgery Department - Dijon (France), [12]CHU Grenoble, Digestive and Visceral Surgery Department - Grenoble (France), [13]CHU Poitier, Digestive and Visceral Surgery Department - Poitier (France), [14]AP-HP, Hopital Saint Antoine, Digestive and Visceral Surgery Department - Paris (France), [15]CHU Clermont Ferrand, Digestive and Visceral Surgery Department - Clermont Ferrand (France), [16]CHU La Timone, Digestive and Visceral Surgery Department, -HM, - Marseille (France), [17]Institut de Cancérologie de l'Ouest Paul Papin - Angers (France), [18]CHU Reims, Digestive and Visceral Surgery Department - Reims (France), [19]Institut Gustave Roussy,Surgical Oncology - Paris (France)

Objectives

Hyperthermic Intraperitoneal Chemotherapy (HIPEC) is as a valuable therapy for selected patients with peritoneal metastasis (PM) from gastric cancer. However, the best chemotherapeutic scheme for HIPEC is unknown. We evaluated postoperative and oncological outcomes after cytoreductive surgery (CRS) and HIPEC in patients with PM from gastric cancer regarding the intraperitoneal (IP) regimen used.

Methods

One hundred eighty patients who underwent CRS and HIPEC in 16 French centers from 1989 to 2014 were included and divided into 4 groups according to the main IP agent used. The log-rank test was used to compare survivals. After adjustments on major cofounding factors that could differ between groups and bias outcomes, Cox models were applied to assess the clinical impact of different regimens.

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Results

Seven drugs protocols were used. IP monochemotherapy was offered to 139 (77.2%) patients and drugs association to 41 (22.8%). Regimens based on mitomycin, oxaliplatin or cisplatin and mitomycin-cisplatin association represented 72 (40%), 56 (31.1%), 28 (15.6%) and 24 (13.3%) patients, respectively. Irinotecan was added to mitomycin or oxaliplatin in 9 patients and doxorubicin to cisplatin in 8.

Morbidity, overall survival (OS) and disease free survivals (DFS) were not significantly influenced by the type of HIPEC drug. Rate of major postoperative morbidity were 51.4%, 48.2%, 53.6% and 66.7% with mitomycin, oxaliplatin, cisplatin or mitomycin-cisplatin, respectively (P = .496). Median OS was 21.2 months with mitomycin, 21.4 months with oxaliplatin, 14.2 months with cisplatin and 13.6 months with mitomycin-cisplatin (P = .313). Multivariate analyses confirmed absence of significant difference for morbidity and OS. Concerning recurrence, median DFS were 12.5, 12.4, 8 and 11.6 months with mitomycin, oxaliplatin, cisplatin or mitomycin-cisplatin, respectively (P = .148). Adjustment and multivariate analyses showed that mitomycin or oxaliplatin significantly enhanced DFS compared to cisplatin (aHR, 2.32; 95% CI, 1.19–4.50). IP drugs association did not significantly influenced OS (median OS: 14 *v* 21, P = .173) or DFS (median DFS 8 *v* 12.4 months, P = .544), compared to monotherapy.

Conclusion

The type of HIPEC drug used for the treatment of gastric cancer with PM does not significantly influence morbidity or OS, neither the use of drugs association. However, best survivals were obtained with mitomycin or oxaliplatin used alone which appeared to significantly enhance DFS compared to cisplatin.

C148

SAFETY AND EFFICACY OF PERIOPERATIVE SYSTEMIC THERAPY WITH CYTOREDUCTIVE SURGERY AND HIPEC VERSUS UPFRONT SURGERY WITH HIPEC ALONE FOR ISOLATED RESECTABLE COLORECTAL PERITONEAL METASTASES: UPDATE OF A MULTICENTRE, OPEN-LABEL, PARALLEL-GROUP, PHASE II-III, RANDOMISED SUPERIORITY STUDY (CAIRO6)

K. Rovers[1], J. Burger[2], R. Wiezer[3], A. Aalbers[4], J. Tuynman[5], S. Radema[6], E. Van Duyn[7], H. Van Grevenstein[8], P. Hemmer[9], P. Tanis[10], C. Punt[11], I. De Hingh[12]

[1]Surgery, Catharina Hospital, Eindhoven - Eindhoven (Netherlands), [2]Surgery, Erasmus University Medical Centre, Rotterdam - Rotterdam (Netherlands), [3]Surgery, St. Antonius Hospital, Nieuwegein - Nieuwegein (Netherlands), [4]Surgery, Netherlands Cancer Institute, Amsterdam - Amsterdam (Netherlands), [5]Surgery, VU University Medical Centre, Amsterdam - Amsterdam (Netherlands), [6]Medical Oncology, Radboud University Medical Centre, Nijmegen - Nijmegen (Netherlands), [7]Surgery, Medisch Spectrum Twente, Enschede - Enschede (Netherlands), [8]Surgery, University Medical Centre Utrecht, Utrecht - Utrecht (Netherlands), [9]Surgery, University Medical Centre Groningen, Groningen - Groningen (Netherlands), [10]Surgery, Academic Medical Centre, Amsterdam - Amsterdam (Netherlands), [11]Medical Oncology, Academic Medical Centre, Amsterdam - Amsterdam (Netherlands), [12]Surgery, Catharina Hospital, Eindhoven - Amsterdam (Netherlands)

Objectives

To compare the safety and efficacy of perioperative systemic therapy and cytoreductive surgery with HIPEC versus upfront cytoreductive surgery with HIPEC alone for isolated resectable colorectal peritoneal metastases.

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Methods

This multicentre, open-label, parellel-group, phase II-III superiority study randomises patients in a 1:1 ratio to perioperative systemic therapy with cytoreductive surgery and HIPEC (experimental arm) versus upfront cytoreductive surgery with HIPEC alone (control arm). Eligible patients are adults with a good performance status (WHO 0-1), histological or cytological proof of a non-appendiceal non-signet ring cell colorectal carcinoma in peritoneal deposits or ascites, resectable disease determined by laparoscopy or laparotomy, no systemic metastases, no contraindications for the planned perioperative systemic therapy, no contraindications for major abdominal surgery, and no systemic therapy within six months prior to randomisation. Perioperative systemic therapy consists of three (capecitabine with oxaliplatin) or four (5-fluorouracil with oxaliplatin or irinotecan) cycles of neoadjuvant chemotherapy with bevacizumab, followed by radiological restaging, followed by one (capecitabine with oxaliplatin) or two (5-fluorouracil with oxaliplatin or irinotecan) additional cycles of neoadjuvant chemotherapy without bevacizumab in case of stable disease or response, followed by four (capecitabine with oxaliplatin or capecitabine monotherapy) or six (5-fluorouracil with oxaliplatin of 5-fluorouracil monotherapy) cycles of adjuvant chemotherapy after cytoreductive surgery with HIPEC. Endpoints of the randomised phase II feasibility and safety study (n = 80) are the feasibility of accrual and the number of patients with severe postoperative complications (Clavien-Dindo >2) up to 90 days after surgery. The primary endpoint of the phase III study is 3-year overall survival, which is hypothesised to be 65% in the experimental arm and 50% in the control arm. Major secondary endpoints are postoperative complications, progression-free survival, quality of life, and costs.

Results

Between September 2017 and April 2018, 41 of the 80 patients of the phase II study have been randomised in 9 centres. If accepted, a study description will be presented at the congress, together with an accrual update and the most important problems in the first study year.

Conclusion

If accepted, a preliminary conclusion regarding the feasibility of accrual is presented at the congress.

C149

THE PRESENCE OF BRAF V600E MUTATION DOESN'T CONTRAINDICATE A CYTOREDUCTIVE SURGERY AND HIPEC IN PATIENTS WITH PERITONEAL METASTASES FROM COLORECTAL CANCER

R. Lo Dico[1], A. Dohan [2], R. Kaci [3], K. Pautrat [1], B. Malgras [1], T. Andre [4], M. Pocard [1]

[1]Department of Oncological Surgery - Lariboisiere Hospital - Inserm U965 Paris 7/Diderot University - Paris (France), [2]Department of Radiology - Cochin Hospital - Inserm U965 Paris 7/Diderot University - Paris (France), [3]Department of Pathology - Lariboisiere Hospital - Inserm U965 Paris 7/Diderot University - Paris (France), [4]Department of Oncology - Saint Antoine Hospital - Paris (France)

Objectives

Overall Survival (OS) in patients with metastatic colorectal cancer (mCRC) containing mutations in BRAF V600E is poor (Franko J, Lancet Oncol. 2016; 12:1709–1719). The benefit of curative resection remains controversial. The aim of this project is to evaluate the OS and disease free survival (DFS) in patients with BRAF V600E mutation treated by cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) with curative intent in order to explore new therapeutic strategies.

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Methods

Patients with peritoneal metastatic colorectal cancer containing mutation in BRAF V600E treated by CRS and HIPEC were collected retrospectively in the database of the surgical department of our hospital. The OS was calculated from the diagnosis of the peritoneal metastases. The DFS was calculated from the date of CRS and HIPEC for the patients undergoing curative surgery, from the diagnosis of the peritoneal metastases for the others.

Results

Between October 2007 and October 2017, 22 patients with peritoneal mCRC containing mutations in BRAF 600E are retrospective collected in this study. Twelve patients received systemic chemotherapy and/or targeted therapy before and after CRS and HIPEC. Mean DFS and OS for the whole cohort were a mean DFS and OS of 25.9 [95%CI: 12.9–38.8] and 53.6 [95%CI: 48.5–58.7] months, respectively.

Conclusion

This study showed an encouraging OS and DFS after CRS and HIPEC in this selected population of mCRC patients with peritoneal metastases and BRAF V600E mutation. The presence of BRAF V600E mutation in this population seems not a contraindication to the CRS surgery and HIPEC with curative intent. Further studies are required to valid of this strategy in this population.

C150

EFFECTS OF NEOADJUVANT INTRAPERITONEAL/SYSTEMIC CHEMOTHERAPY (NIPS) ON PERITONEAL METASTASIS AND LYMPH NODE METASTASIS OF GASTRIC CANCER

Y. Yonemura

Japanese/Asian School of Peritoneal Surface Maligancy Treatment, Kishiwada Tokusyukai and Kusatsu general Hospital - Kyoto (Japan)

Objectives

Methods

Exploratory laparoscopy (EL) was performed in 107 gastric cancer (GC) patients with peritoneal metastasis (PM) and PCI and cytology was determined. Then, a peritoneal port system was introduced into the abdominal cavity, and then a series of 3-week cycles of NIPS was performed (NIPS Group). Specifically, S1 was administered orally twice daily at a dose of 60 mg/m^2/day for 14 consecutive days, followed by 7 days rest. Docetaxel and cisplatin were administered intraperitoneally (i.p. 30 mg/m^2 on day 1) with. 500 ml of normal saline. The same dose of docetaxel and cisplatin were administered intravenously (i.v.) on day 8. The treatment course was repeated every 3 weeks for 3 courses. Four weeks after last cycle of NIPS, laparotomy for cytoreductive surgery and HIPEC were done, and PCI and cytologic changes were studied. As a control group, 240 GC patients with PM underwent D2-gatrectomy without NIPS (non NIPS group).

Results

Mean PCI before NIPS and after 3 cycles of NIPS were 10.3 and 7.2 (P-0.004).

Positive cytology before NIPS became negative in 69% of patients after NIPS.

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Mean total number of metastatic lymph node (TNML) of NIPS and non NIPS Group was 4.6 (0–29) and 14.8 (0–82), In non NIPS Group, pN1, pN2, pN3 were 10%, 21%, 38% and 30%. In NIPS Group, those were 37%, 22%, 36% and 5%, respectively. There was a significant difference in the grade of LN metastasis between the two groups. Five year survival rate of N0, N1-2, N3 (NIPS Group) were 12%, 8% and 0%.

Survival of NIPS Group was significantly better than non-NIPS Group (P = 0.0001).

Conclusion

NIPS was effective for the reduction of PCI and cytological status. Additionally, NIPS reduced TNML and grade of LN metastasis. Regional LN metastases were explored with high concentration of anticancer drugs absorbed from omental milky spots. D2 dissection including No, 7 8, and 9 LN is recommended when total gastrectomy and peritonectomy are performed.

C151

PATTERNS OF ABDOMINAL SURFACE THERMOGRAPHY IMAGING DURING CLOSED HIPEC

P. Schredl[1], A. Dinnewitzer[1], D. Neureiter[2], S. Ciftci[1], M. Fallaha[3], J. Holzinger[1], K. Emmanuel[1], T. Jäger[1]

[1]Department of Surgery, Paracelsus Medical University - Salzburg (Austria), [2]Institute of Pathology, Paracelsus Medical University - Salzburg (Austria), [3]Faculty of Medicine, Imperial College School of Medicine - London (United Kingdom)

Objectives

Temperature control is an important pillar of hyperthermic intraperitoneal chemotherapy (HIPEC). An instantaneous, non-contact and non-invasive temperature monitoring of the abdominal surface during closed HIPEC may be implemented by infrared thermography (IRT) as an add-on or an alternative to intraabdominal temperature monitoring with temperature probes. The aim of our study was to provide novel data of the abdominal surface temperature distribution assessed by infrared thermography during closed HIPEC.

Methods

Temperature of five abdominal surface regions (right hypochondriac [RH], left hypochondriac [LH], left iliac [LI], right iliac [RI], and umbilical [UM]) were assessed in 5-minute intervals over 30 minutes in 16, and over 60 minutes in 17 patients during closed HIPEC. Temporal and spatial trends of abdominal surface temperature patterns were assessed by panel data analysis. During the closed HIPEC procedure primary temperature control was assessed with three intraabdominal, one inflow, and one outflow temperature probes.

Results

In total 1240 temperature points over 5 abdominal surface regions (each 248 points) over 30 to 60 minutes in 33 patients were assessed with infrared thermography. The mean temperature overall points were 33.5 ± 0.4. The detailed mean temperatures of the different abdominal regions were: RH: 33.8 ± 1.7, LH: 34.0 ± 1.5; LI; 34.1 ± 2.2; RI: 33.8 ± 1.8; UM: 32.0 ± 2.5.

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Conclusion

Our preliminary results suggest the feasibility of infrared thermography as an add-on in temperature control during closed HIPEC. We will present omissions and pitfalls together with inference statistics correlating the abdominal surface temperature assessed by infrared thermography with the corresponding temperature of the probes at the 11th international workshop on peritoneal surface malignancy 2018 in Paris.

C152

EPIDEMIOLOGY AND SURVIVAL IMPACT OF SYNCHRONOUS PERITONEAL METASTASES OF EPITHELIAL MALIGNANCIES: A NATIONWIDE POPULATION-BASED OBSERVATIONAL STUDY

K. Rovers[1], P. Vissers[2], L. Vaartjes[1], T. Van Oudheusden[1], W. Van Driel[3], J. De Wilt[4], J. Burger[5], P. Tanis[6], N. Kok[7], V. Lemmens[8], I. De Hingh[1]

[1]Surgery, Catharina Hospital, Eindhoven - Eindhoven (Netherlands), [2]Research, Netherlands Comprehensive Cancer Organisation, Eindhoven - Eindhoven (Netherlands), [3]Gynaecology, Netherlands Cancer Institute, Amsterdam - Amsterdam (Netherlands), [4]Surgery, Radboud University Medical Centre, Nijmegen - Nijmegen (Netherlands), [5]Surgery, Erasmus University Medical Centre, Rotterdam - Rotterdam (Netherlands), [6]Surgery, Academic Medical Centre, Amsterdam - Amsterdam (Netherlands), [7]Surgery, Netherlands Cancer Institute, Amsterdam - Amsterdam (Netherlands), [8]Research, Netherlands Comprehensive Cancer Organisation, Utrecht - Utrecht (Netherlands)

Objectives

To provide comprehensive nationwide data on the epidemiology and survival impact of synchronous peritoneal metastases of epithelial malignancies.

Methods

In all consecutively diagnosed epithelial malignancies (Netherlands Cancer Registry, nationwide, 2008–2014), we determined the European age-standardised incidence and the distribution of origins of synchronous peritoneal metastases. For each origin, the incidence proportion of (isolated) synchronous peritoneal metastases was determined and the overall survival of patients with synchronous peritoneal metastases was compared with that of synchronous non-peritoneal metastases by using multivariable Cox regression analysis.

Results

Of 469.586 epithelial malignancies, 14.165 presented with synchronous peritoneal metastases (3%, 15% of metastatic epithelial malignancies). The age-standardised incidence of synchronous peritoneal metastases of epithelial malignancies was 11.0/100.000 person-years. Primary locations were ovary (28%), colon (23%), stomach (12%), pancreas (8%), and others (29%, 22 locations). Incidence proportions ranged from <1%–62% (breast-ovary). Overall survival was worse for patients with synchronous peritoneal metastases versus synchronous non-peritoneal metastases (hazard ratio [HR] 1.21 [95% confidence interval (CI) 1.18–1.24]), with positive subgroup analyses in metastatic epithelial malignancies of colon, stomach, pancreas, lung, rectum, esophagus, urinary tract, breast, kidney, and unknown origin (HR>1.00 [95%CI > 1.00]).

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Conclusion

The high total incidence, relevant incidence proportions in numerous primaries, and dismal prognostic impact underscore that synchronous peritoneal metastases of epithelial malignancies remain a major challenge.

C153

ROLE OF PERIOPERATIVE CHEMOTHERAPY (PC) WITH CYTOREDUCTIVE SURGERY (CRS) AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) FOR COLORECTAL CANCER (CRC) CARCINOMATOSIS

N. Hana, A. Hanna, C. Boutros, D. Hanna

University of Maryland School of Medicine - Baltimore (United States)

Objectives

To evaluate the survival benefit of PC in patients undergoing CRS and HIPEC for CRC carcinomatosis.

CRS and HIPEC in CRC carcinomatosis have been shown to improve survival in selected patients with good performance status, and low peritoneal cancer index (PCI) undergoing complete cytoreduction. However, the lack of randomized clinical trials addressing the role of PC in these patients is lacking. We conducted a retrospective analysis of prospectively maintained database to evaluate the survival benefit associated with PC in CRC patients selected for CRS and HIPEC at our institution.

Methods

Between 12/2004 and 12/2016, 94 patients with carcinomatosis from CRC underwent CRS and HIPEC at our center. Data were retrospectively collected under IRB approval. Effect of PC on overall survival (OS) was assessed using univariate and multivariate Cox regression analysis.

Results

The mean age of the study cohort was 54 years (±15.9), 52% were males, and 63% were of White ethnicity. The mean peritoneal carcinomatosis index was 14.2 (range 1–33) and a CCR of 0 or 1 was achieved in 94% of patients. Neoadjuvant chemotherapy was administered to 48% patients, 44% also received bevacizumab, and 59% received adjuvant chemotherapy. The mean operative time was 7 (±2) hours. The median length of stay was 7 days (IQR 6–11 days) and 28% suffered a complication. A Clavien Dindo complication score of 3 or 4 occurred in 4 patients (6%) and 2 patients (3%) died in the perioperative period. The median actuarial overall survival (OS) was 43.8 months (IQR = 18.5–83.7 months). After multivariate Cox regression the receipt of neoadjuvant, adjuvant or any perioperative chemotherapy was not associated with a difference in OS ($p > 0.05$). This also held true in subset analyses by mucinous histology.

Conclusion

There was no survival advantage of perioperative chemotherapy amongst patients undergoing CRS and HIPEC for colorectal carcinomatosis.

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C154
UNDERUTILIZATION OF AGGRESSIVE TREATMENT APPROACHES IN PATIENTS WITH COLORECTAL AND GASTRIC PERITONEAL CARCINOMATOSIS-ANALYSIS OF THE NATIONAL CANCER DATABASE

G. Salti, S. Naffouje

Division of Surgical Oncology, the University of Illinois at Chicago - Chicago (United States)

Objectives

Several gastrointestinal and gynecological malignancies have the potential to disseminate within the peritoneal cavity as peritoneal carcinomatosis (PC) which has been shown to significantly decrease overall survival. Multimodal approaches combining aggressive cytoreductive surgery, intraperitoneal hyperthermic chemotherapy and systemic chemotherapy have been proposed and have shown promise in improving patient outcomes.

The aim of this study is evaluate ‘aggressive’ treatment approach (radical debulking surgery with chemotherapy) in colorectal (CRC) and gastric PC patients in comparison to the accepted and standard approach in ovarian PC in the United States. Data were obtained from the National Cancer Database (NCDB) during the years 2004–2014.

Results

There was a total 1,122,038 patients with ovarian, CRC, and gastric cancers treated during this period. Of these, 52,953 patients had PC only (27,552 ovarian; 5,293 CRC; 20,108 gastric). None of these patients had other intra-abdominal or extra-abdominal metastases. In ovarian PC, 48.5% had radical debulking surgery plus chemotherapy with a median survival of 33.6 months. This compares to only 2.6% in CRC (median survival, 24 mo) and 2.8% in gastric PC (median survival, 13.7 mo). Debulking surgery with chemotherapy offered all patients groups significantly improved survival compared to debulking alone or systemic therapy alone ($P = 0.000$).

Conclusion

These data suggest that a high proportion of U.S. patients with CRC and gastric carcinoma PC do not receive surgical treatment and that when aggressive surgical approach plus chemotherapy is utilized, patient outcome is significantly improved. Better education and patient stratification is thus warranted.

C155
PROGNOSTIC VARIABLES IN COLORECTAL PERITONEAL CARCINOMATOSIS: AN EVALUATION OF A SINGLE ASIAN CENTRE’S EXPERIENCE

W.L. Loh, H.C.G. Tan, S.C. Chia, C.A.J. Ong, C.C.M. Teo

National Cancer Centre Singapore - Singapore (Singapore)

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Objectives

The peritoneum is the only site of metastatic disease in approximately 10–15% of patients with colorectal cancer, and carries a poorer prognosis compared with metastasis in other visceral organs. In highly selected patients, cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) has been shown to offer long-term disease-free and overall survival for an otherwise terminal disease. We describe our experience with CRS-HIPEC for colorectal peritoneal metastases (CPM) and identify prognostic factors for survival.

Methods

A retrospective study of a prospectively maintained database at the National Cancer Centre Singapore was performed. Patients underwent CRS-HIPEC from January 2005 to December 2017. Our endpoints were overall survival (OS) and disease-free survival (DFS), with prognostic factors being the secondary outcome.

Results

A total of 104 cases (64 female) were included, of which 25% were cases of synchronous CPM. Variables analysed included demographic data, medical co-morbidities, primary tumour variables (histology, size, grade, nodal status), synchronicity of peritoneal metastases, serum tumour marker levels, presence of multivisceral resection use of neoadjuvant or adjuvant therapy, Peritoneal Carcinomatosis Index (PCI), presence of ascites, need for enterostomy(ies), estimated blood loss, use of early post-operative intraperitoneal chemotherapy (EPIC), length of stay (intensive care unit and total hospitalisation), and presence of complications. The median age of patients was 55 (range 14–76), PCI was 7 (range 0–31), and the majority (97%) of patients achieved complete cytoreduction. A total of 16 cases received neoadjuvant therapy prior to surgery and 25 cases proceeded on to adjuvant systemic therapy. The median OS was 40.9 months (range 33–48), and median DFS was 14.0 months (range 13–22). The 1-year, 3-year, and 5-year OS and DFS rates were 90.4%, 60.5%, 29.5% and 56.8%, 12.8%, 12.8% respectively. On multivariate analysis, PCI was the only variable significant for OS, and post-CRS adjuvant therapy was the only variable significant for DFS.

Conclusion

Long-term OS and DFS is possible in a select group of patients with CPM. PCI remains the most prognostic for OS, while the addition of adjuvant therapy prolonged DFS but did not significantly affect OS, indicating that ultimately, tumour biology and burden may be more important in OS.