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The Clinical Outcome in Patients with Peritoneal Metastasis

Spiliotis J[1,2,3]*, Farmakis D[1], Raptis A[2], Kopanakis N[3], Charalampopoulos E[1] , Tshijanou F[2], Margari H[2], Karachalios D[1], Christopoulou A[4]

[1]European Interbalkan Medical Center, Thessaloniki Greece

[2]Athens Medical Center, Marousi Greece

[3]Metaxa Cancer Memorial Hospital, Piraeus Greece

[4]St. Andreas Hospital, Patras Greece

ABSTRACT

Cytroreductive surgery (CRS) and HIPEC are controversial effective treatment options for selected patients with peritoneal metastases. We retrospectively examined 4.500 patients with peritoneal metastases from different tumors from 2005 to 2020. Patients were divided in 4 groups, surgery plus HIPEC and then systemic chemotherapy: Group A n=730, Group B n=700, R_0 surgery plus systemic chemotherapy, Group C n=870, palliative surgery plus systemic chemotherapy and Group D n=2.200, palliative care and best support. The postoperative outcomes, morbidity, mortality were compared between the 4 groups. The mean survival rates Group A=24,4+10,2m, Group B= 18,4+6,3m, Group C=12,3+5,7m, Group D=5,8+2,3m ($p<0.05$ between Gr A vr Gr B).

There was no statistically significant difference in the 30-day mortality and morbidity. In conclusion CRS + HIPEC are feasible in 16% of our patients with peritoneal metastases and are associated with pro-longed survival.

***Corresponding author**

Spiliotis John, European Interbalkan Medical Center Asklipiou 10, 57001 Pilaia, Thessaloniki, Greece E-mail: jspil@hotmail.gr

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Introduction

The management of peritoneal metastasis remains a difficult problem. The prognosis is poor and represents the spread of malignancies to parietal and visceral peritoneum. With the multi-disciplinary approach of cytoreductive surgery (CRS) and hyper thermic intraperitoneal chemotherapy (HIPEC) in appropriately selected patients long term survival is achievable [1-3].

The main goals: CRS aims to remove all visible tumor cells, the HIPEC procedure is based on the principle that a high concentration of chemotherapy in peritoneal cavity can eradicate the non-visible malignant cells. The outcome of CRS and HIPEC depends on the tumor extent and the completeness of cytoreduction and also the tumor origin (biology) [4].

Materials and Methods

Over the past 15 years the same group of surgeons under the same peritoneal surface malignancy program, initiated and directed by the same person (J.S.), have recruited patients with peritoneal metastasis and have prospectively registered and studied these cases. The departments are national referral centers and since 2015 European referral centers for CRS + HIPEC.

Inclusion Criteria

Patients eligible for CRS + HIPEC were those with pm from ovarian (recurrent, residual or primary) colorectal cancer with PCI <17 peritoneal mesothelioma, appendicle neoplasms, gastric cancer with PCI<12 and rare tumors with low PCI<10.

Exclusion Criteria

Exclusion criteria were (a) Age >75years, (b) ASA score >3, (c) extra peritoneal disease, (d) massive disease involvement in small bower, (e) disease involvement in hepatic pedicle or the pancreas, (f) invasion of retroperitoneal space, (g) more than 3 stenosis of the small bowel. Preoperative assessment included CT, magnetic enteroclysis, PET/CT, gastroscopy, colonoscopy and decisions are finalized in multi-disciplinary team meetings. From August 2005 to August 2020 4.500 were introduced in the program.

Statistics

Overall survival was estimated using the Kaplan Meier method with long rank test and chi-square test was used to estimate the significance between two medians. A p value <0.05 was considered as statistically significant.

Results

4.500 patients were assessed for treatment. Of them 730 patients (16,2%) were included in the CRS+HIPEC+postoperative systemic chemotherapy (Group A). And their mean overall survival was 24,4+10, 2 months. Another group of 700 patients (15,5%) were performed complete CC0cytoreduction and postoperative systemic chemotherapy (Group B). Their meanoverall survival was 18, 2+6,3 months.

The next group with 870 patients (19,3%) were performed palliative surgery CC1, CC2 or CC3 and then postoperative chemotherapy (Group C). Their mean overall survival was 12,3+5,7 months.

The remaining 2.200 patients (48,8%) were excluded from aggressive procedures, received palliative salvage chemotherapy and best support care (Group D). Their mean overall survival was 5,8+2,3 months (table 1).

Table 1

TREATMENT OPTIONS AND MEAN SURVIVAL RATES IN THE 4 GROUPS		
GROUP	N	MEAN SURVIVAL MONTH
A	730 (16,2%)	24,4+10,2m
B	700 (15,5%)	18,2+6,3m
C	870 (19,3%)	12,3+5,7m
D	2200 (48,8%)	5,8+2,3m

There is a statistically significance difference between group A and B ($p<0.05$) and also between B vs C ($p<0.05$).

The better survival rates are observed in patients with peritoneal metastasesfrom mestotheliomas, ovarian, appendiceal neoplasms, colon cancer and gastric according the mean survival rates depending the tumor location and histology. The overall survival in 1st, 3rd, 5th, 7th and 10th year are presented in table 2. The morbidity and mortality rates are presented in table 3.The morbidity is between 35% to 48% among the groups, not statistical sign. On the other hand the mortality is higher in HIPEC group (group A) and statistically significant between group A vs groups C andD ($p<0.05$).

TABLE 2

SURVIVAL RATES BETWEEN THE GROUPS				
SURVIVAL	**Gr A**	**Gr B**	**Gr C**	**Gr D**
1 year	83%	70%	42%	12%
3 years	54%	41%	16%	5%
5 years	22%	13%	8%	0
7 years	18%	4%	2%	0
10 years	9%	0	0	0

TABLE 3

MORBIDITY AND MORTALITY RATES BETWEEN THE 4 GROUPS		
GROUP	**MORBIDITY**	**MORTALITY**
A	48%	4,9%
B	39%	4,0%
C	35%	3,6%
D	45%	2,1%

The quality of life (QOL) in Karnofsky scale between the groups is presented in table 4.

The PCI index between groups is presented in table 5. There is a statistically significant difference ($p<0.05$) between group A and other groups.

TABLE 4

QOL ACCORDING KARNOFSKY SCALE BETWEEN THE 4 GROUPS				
GROUP	**1 YEAR**	**3 YEARS**	**5 YEARS**	**10 YEARS**
A	90	70	70	50
B	80	70	-	-
C	70	50	-	-
D	50	-	-	-

TABLE 5

PERITONEAL CANCER INDEX, MEAN VALUES BETWEEN 4 GROUPS	
GROUP	PCI MEAN VALUE
A	12,7+6,1m
B	20,4+7,3m
C	26,8+8,6m
D	31,8+5,2m

Discussion

Peritoneal metastasis (PM) represents advanced malignant disease and has generally been associated with a grim prognosis. Although PM is categorized as metastatic disease, it represents a special disease pattern considered to be logo regional limited to the abdominal cavity [5-7].

Cytoreductive surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) have been used as logo regional treatment for selected patients and a long term survival is achievable [8].

On the other hand patients not meeting the inclusion criteria for CRS and HIPEC represent a group with advanced PM. Most of these patients have a rapid, fatal clinical course.

Our results showed a mean survival in the CC0 group of 18,2 +6,3 months and in CC1,2,3 groups of 12,3+5,7 months.

These findings are comparable to results reported by Rodt et al, who reported a median survival of 12,7 months [9].

Concerning the patients treated with palliative best support treatment in our study the mean survival was 5,8+2,3 months.

This result is inferior to our previous study with preliminary results from 450 patients and the results by Hompes et al, who found a median survival of 9,5 months for patients with PM who received systemic chemotherapy [10,11].

The most important factors concerning the overall survival in patients with PM is the tumor histology (appendiceal neoplasms), the completeness of cytoreduction (CC), the response to neo-adjuvant chemotherapy and the peritoneal cancer index (PCI) less than 15{7}.

The prognostic relevance of the CC score and the PCI was evaluated by Elias etal in 523 patients [12]. In multivariate analysis they found that CC and PCI are strongly correlated with overall survival. Our study demonstrates a 30 day mortality rate varying between 2,1% to 4,9% with no statistical significance between the groups.

In our patients who were excluded from the HIPEC group represented a group of patients with a very high PCI index (table 5) which was statistically different from the PCI in the HIPEC group. The most important information from our study is the crucial role of CRSwhich is demonstrated with previous studies in ovarian cancer and in colorectal cancer [13,14].

On the other hand the implementation of HIPEC in complete cytoreductive surgery rose up the survival rates from 18,2+6,3 months to 24,4+10,2 months. A prospective trial found that an overall survival of 12, 6 months for 50 patients with PM randomized to standard care treatment with simple chemo regimens versus new drugs and targeted therapies [15].

Our study suggests that patients with PM must be evaluated by a multi- disciplinary team in order to assess with objective criteria the candidates for CRS + HIPEC.

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