

# Locoregional treatment of peritoneal sarcomatosis

## A single-centre experience



Ann. Ital. Chir., 2016 87: 333-336  
pii: S0003469X16025240

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### Locoregional Treatment of Peritoneal Sarcomatosis. A single-centre experience

**BACKGROUND:** Peritoneal sarcomatosis appears to be responding poorly to systemic chemotherapy. Treatment options traditionally include surgical resections, chemotherapy and radiation therapy. Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) offers a promising alternative locoregional treatment option.

**PATIENTS AND METHODS:** We examine retrospectively 8 patients (4 females, 4 males) with peritoneal sarcomatosis. The most common histology type was the liposarcoma (4/8). The chemotherapeutic agents that were administered were mitomycin, cisplatin and doxorubicin. We analyse our cases with regard to the PCI, the CC score, the complications that occurred and the overall survival.

**RESULTS:** A complete level of cytoreduction (CC0/1) was feasible in 5/8 of patients. We report post-operative complications such as GI leaks and fistulas in 3 cases and infections in 2 cases. Overall survival was proved to depend on the PCI (better overall survival rate when  $PCI < 20$ )

**DISCUSSION:** We identify acceptable morbidity, comparable to other series of patients undergoing CRS+HIPEC for other histologies. The specific sarcoma type and the previous treatment received prove to be factors that alter significantly the prognosis and the survival rates: therefore, conclusions cannot be safely excluded in such small patient series. On the whole, we conclude that, given the already positive and promising results from CRS+HIPEC in sarcomatosis, more studies need to be performed, in order to determine the role of all the aforementioned factors.

**KEY WORDS:** Fibrosarcoma, HIPEC, Leiomyosarcoma, Liposarcoma, Rabdomyosarcoma, Sarcomatosis

### Introduction

Soft tissue sarcomas are regarded as a family of sarcomas that may arise from any site, with the most common sites of origin being the extremities and the abdomen/retroperitoneum.

Surgical resection and adjuvant systemic chemotherapy, with or without radiotherapy, is the most commonly chosen treatment; nevertheless, this choice results in a high recurrence rate, from which 80-90% involve multifocal intra-abdominal dissemination<sup>1,2</sup>.

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is a multimodality treatment that employs high locoregional concentration of chemotherapeutic agents, heated at 42,5 °C, in order to achieve increased cytotoxicity. Unfortunately, the experience of using CRS+HIPEC on peritoneal sarcomatosis may be described as limited<sup>3,4</sup>.

In this retrospective analysis, we present the experience gained in our centre, from performing CRS+HIPEC in patients with sarcomatosis.

Pervenuto in Redazione Gennaio 2016. Accettato per la pubblicazione Aprile 2016

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## Patients and Methods

We examine 8 patients with peritoneal sarcomatosis, that were referred to our centre, throughout a ten-year period. All patients underwent radical cytoreduction, as previously described by Sugarbaker <sup>5</sup>, including peritonectomy procedures and organ resections, in order to achieve complete cytoreduction, between others.

The extent of intra-abdominal distribution of the disease was assessed in the OR, with the use of the Peritoneal Cancer Index (PCI) <sup>6</sup>.

The completeness of cytoreduction score (CCs) was also used, in order to determine the residual disease after cytoreduction.

In more detail, the score was calculated as following:

- Zero (0) represents **no visible residual disease**
- One (1) represents **residual tumor nodules < 2,5 mm**
- Two (2) represents **residual tumor nodules < 2,5 cm**
- Three (3) represents **residual tumor nodules > 2,5 cm**

CC<sub>0/1</sub> is considered as adequate cytoreduction <sup>7,8</sup>.

Hyperthermic Intraperitoneal Chemotherapy (HIPEC) was performed after cytoreduction, with the closed abdomen perfusion technique, by administering 3 liters of perfusate (N/S and chemotherapeutic agent), warmed at 42.5°C.

Tumor histology may be observed in Table IV.

As far as the chemotherapeutic agents are concerned, the majority of our patients (5/8) received 40mg/m<sup>2</sup> of mitomycin for 60 minutes, two patients received 15mg/m<sup>2</sup> of doxorubicin for 90 minutes and one patient received 150mg/m<sup>2</sup> of cisplatin for 60 minutes.

Our statistical analysis, mainly due to the small amount of cases, tries to investigate only the relation between the PCI, as a marker of cancer distribution, and the overall survival.

## Results

Our patients were equal as far as gender is concerned (4 males, 4 females), with a median age of 48,8 years old, ranging from 20 to 70.

TABLE I - Pre-operative Information

	N (Total: 8)	%
Site of origin		
Pelvis	3	37,5%
Retroperitoneal	5	62,5%
Initial treatment		
Surgical Resection	2	25%
Surgical Resection + Chemotherapy	2	25%
Surgical Resection + Radiotherapy	4	50%

The majority of the tumors we dealt with originated from the retroperitoneum (5/8), with the rest originating from the pelvis, whilst most of them had received a combination of surgical treatment, chemotherapy and radiation therapy before showing up in our centre (Table I).

In half of the cases, we were able to achieve a CC<sub>0</sub> level of cytoreduction, whilst an adequate cytoreduction (CC<sub>0/1</sub>) was feasible in a total of 5 cases (Table II).

Cytoreductive procedures may be clearly observed in Table III, and involved 6 omentectomies, 4 large and 4 small bowel resections and 3 diaphragmatic resections, between others.

Finally, in Table IV we present an overall table with specific information on PCI and CC score of each patient, along with the disease-free survival and the overall survival.

TABLE II - Completeness of Cytoreduction

Score	N (Total: 8)	%
CC <sub>0</sub>	4	50%
CC <sub>1</sub>	1	12,5%
CC <sub>2</sub>	2	25%
CC <sub>3</sub>	1	12,5%

TABLE III - Peritonectomies and visceral resections

Procedure	N (Total:8)	%
Omentectomy	6	75%
Large Bowel Resection	4	50%
Small Bowel Resection	4	50%
Diaphragmatic Resections	3	37,5%
Hysterectomy	2	25%
Hepatic Resection/ RFA	1	12,5%
Splenectomy	1	12,5%

TABLE IV - Disease-Free Survival and Overall Survival

Gender	Age	Histology	PCI	CC	DFS (months)	OS (months)
F	66	Liposarcoma	8	0	29	40
F	42	Leiomyosarcoma	14	1	0	33
M	38	Liposarcoma	39	2	0	12
F	44	Fibrosarcoma	30	1	0	4
M	20	Rabdomyosarcoma	33	2	0	12
F	48	Leiomyosarcoma	7	0	16	28
M	70	Liposarcoma	10	0	8	8
M	63	Liposarcoma	10	0	12	12

## Discussion

The experience available for the treatment of peritoneal sarcomatosis with cytoreductive surgery and HIPEC may be characterised as limited. Nevertheless, some promising results have been recently published concerning pediatric intrabdominal sarcomatosis, which suggest a benefit from CRS and HIPEC in such cases<sup>9</sup>.

In our study, we present our experience from performing CRS and HIPEC in patients with sarcomatosis.

To start with, we observed an acceptable complication rate, comparable to our other series of patients undergoing CRS and HIPEC<sup>10</sup>. Specifically, we encountered 3 GI leaks/fistulas and 2 infections (one post-op pneumonia and one catheter-related bloodstream infection).

The aspect that shows the most interest for our team concerns the overall survival and the disease-free survival. It appeared hard to compare survival rates with other studies, as there is a wide range for these rates, mainly due to different factors that are present in each series. Briefly, the presence of prior surgical treatment or chemotherapy or radiation therapy or combinations of these treatments may alter the overall survival rate and the disease-free survival rate. More importantly though, it is noted by a number of studies that the differences in histology types of tumors may alter significantly the prognosis, the success of treatment and, therefore, survival rates<sup>11-13</sup>. It has been described that leiomyosarcomas are accompanied by the best survival of all, whereas poorly differentiated sarcomas are accompanied by the worst<sup>14-16</sup>.

The most easily extracted conclusion regards the correlation between PCI and overall survival. We were able to determine that the overall survival of patients with PCI<20 differs significantly and is better, than this of patients with PCI>20 (Fig. 1).

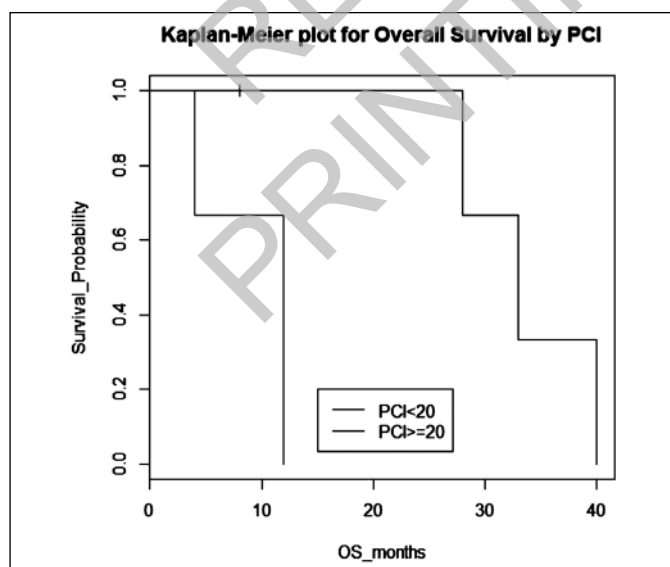


Fig. 1: Overall Survival for PCI.

However, at this point, we have to mention that, as it has already been pointed out by Randle et al<sup>17</sup>, the median survival for patients with peritoneal sarcomatosis that receive CRS and HIPEC turns out to be similar with the one described by Karakousis et al<sup>2</sup> from 1992, long before the induction of our method in the treatment of sarcomatosis.

Therefore, we conclude that CRS and HIPEC may be applied in cases of sarcomatosis with comparable morbidity and mortality rates to other histologies and cancer origins. Thus, many more studies need to be conducted in order to have more definitive and substantial conclusions. We consider that separate studies for each histology type need to be performed, as it appears to play a major role in the prognosis and outcome. Also, more light should be shed in the outcomes with regard to the presence of prior treatments.

Finally, we propose that such studies need to be performed by high-volume reference centres, with significant experience in performing CRS and HIPEC, in pre-operative patient assessment and in post-operative follow-up and complication treatment.

## Riassunto

La sarcomatosi peritoneale appare scarsamente sensibile alla chemioterapia sistemica. I trattamenti tradizionali comprendono le resezioni chirurgiche, la chemioterapia e la radioterapia. La chirurgia citoreducente (CRS) e la chemioterapia ipertermica intraperitoneale (HIPEC) rappresentano delle promettenti opzioni di trattamento locoregionale.

Abbiamo esaminato retrospettivamente 8 pazienti (4 donne e 4 uomini) affetti da sarcomatosi peritoneale, e in 4 pazienti su 8 istologicamente erano rappresentati da liposarcoma. I farmaci chemioterapici somministrati erano stati mitomicina, cisplatino e doxorubicina.

Esaminiamo ora questi casi riguardo il Peritoneal Cancer Index (PCI), il grado di completezza della citoreduzione (CC), le complicazioni verificatesi e la sopravvivenza generale.

La citoreduzione completa (CC<sub>0/1</sub>) è stata possibile in 5 pazienti su 8. Le complicazioni postoperatorie, quali la deiscenza anastomotica del tratto digestivo, con fistolizzazione in 3 casi, e l'infezione in 2 casi. La sopravvivenza globale è risultata dipendente dall'indice neoplastico peritoneale (PCI), la migliore in caso di PCI<20). Si riconosce una morbilità accettabile, paragonabile ad altre casistiche di pazienti sottoposti a CRS+HIPEC per altri tipi istologici. Il tipo specifico di sarcoma ed il trattamento ricevuto in precedenza hanno dimostrato di rappresentare fattori in grado di modificare in modo significativo la prognosi ed il tasso di sopravvivenza: peraltro non si possono trarre con certezza conclusioni basate su un così limitato numero di pazienti.

Nel complesso concludiamo che, dati i risultati già posi-

tivi e promettenti della CRS+HIPEC nella sarcomatosi, sono necessari ulteriori studi per accertare il ruolo di tutti i fattori presi in considerazione.

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