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Article

2011

Published version

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Ris, Frédéric; Herren, Gilles Marc Daniel; Morel, Philippe; Volonte, Francesco Giorgio Domenic; Roth, Arnaud; Huber, Olivier

### How to cite

RIS, Frédéric et al. Management of peritoneal carcinomatosis by surgical cytoreduction and hyperthermic intraperitoneal chemotherapy. In: Swiss knife, 2011, vol. 8, n° 1, p. 16.

This publication URL: <https://archive-ouverte.unige.ch/unige:25856>

# Management of peritoneal carcinomatosis by surgical cytoreduction and hyperthermic intraperitoneal chemotherapy

Peritoneal carcinomatosis (PC) is a common manifestation of advanced malignancies, associated to dismal prognosis.

Frédéric Ris, frederic.ris@hcuge.ch  
Gilles Herren, herren7@gmail.com  
Philippe Morel, philippe.morel@hcuge.ch

Francesco Volonté, francesco.volonte@hcuge.ch  
Arnaud Roth, arnaud.roth@hcuge.ch  
Olivier Huber, olivier.huber@hcuge.ch

**PC was considered in the past decade as a terminal condition, with an overall median survival of 3.1-6 month with palliative treatment<sup>1,2</sup>. There is presently increasing interest in hyperthermic intraperitoneal chemotherapy (HIPEC) combined with surgical cytoreduction (SC). SC-HIPEC is used in some centers to treat PC due to cancers of the appendix (pseudomyxoma), stomach, colo-rectum, ovaries and of the peritoneal serosa (mesothelioma). We report here the general principles of SC-HIPEC and some aspects of our results with this procedure.**

Spratt described in 1980<sup>3</sup> the first use of SC-HIPEC for a recurrent pseudomyxoma. Sugarbaker's and Gilly's groups<sup>4-6</sup> started to develop interest in local HIPEC after extended debulking, so called surgical cytoreduction (SC)<sup>5</sup>. HIPEC seemed to be effective in well selected patients, but was associated to high morbidity and mortality rates<sup>7</sup>.

The concept of this procedure is to administer to the abdominal cavity, after complete or near-complete SC, a high local concentration of cytotoxic agents, mainly mitomycin C or cisplatin. The efficacy of chemotherapy is potentialized by hyperthermia (42°)<sup>8</sup>, but is associated to low systemic toxicity due to the slow diffusion through the peritoneo-plasmatic barrier<sup>9</sup>.

## Scores in peritoneal carcinomatosis

The anatomical extension of the disease in the peritoneal cavity is best evaluated by the peritoneal carcinomatosis index (PCI) described by Sugarbaker (figure 1). Briefly, the abdomen is divided into 13 areas, each of which is assigned a score of 0 to 3 on the basis of the size of the encountered lesions (total score range:1-39)<sup>10</sup>. Other scores were proposed, which are similar to PCI but have not achieved its general acceptance<sup>11</sup>. PCI should be computed before and after SC. The initial PCI has been shown to have a very strong prognostic value. According to the primary tumor, cut-off PCI values have even been proposed to help to select patients for SC-HIPEC (Table 1).

For other primaries, cut-off values are still to be defined. Finally, the completeness of cytoreduction was also shown to have a very strong prognostic value: it is best evaluated by the post-resection PCI, which should tend to zero. Long-term results are so much worse after incomplete SC (Table 1), that there is now general agreement to give up all thoughts of SC-HIPEC when initial exploration demonstrates irresectable disease. Indications: Table 1 summarize the current indications and results for SC-HIPEC after complete or incomplete resection, with cut-off values of PCI when available.

## Patient selection

Three factors are mandatory to perform a SC-HIPEC:

1. Careful analysis of the extension of the disease with estimation of the pre-operative PCI score (with cut-off values for some pathologies); PC should seem fully resectable

2. Good general condition of the patient, according to the high morbidity of the procedure
3. Informed consent for a high-risk procedure which is still lacking definitive proof of efficacy (with the notable exception of PC arising from colon cancer<sup>16</sup>)

After extensive cytoreduction, which can take 10 or 12 hours of effort, HIPEC is performed. To be effective, chemotherapy should diffuse in all recesses of the abdominal cavity, with a homogenous temperature close to 42°. Two techniques are currently used: the so-called Coliseum technique (open technique)<sup>12</sup> and the closed technique<sup>2</sup>. Overall, no difference in terms of efficacy was shown between these two techniques in published series.

## Morbidity

According to recent publications, overall operative mortality of SC-HIPEC is in the range of 1-12%. Postoperative morbidity of this procedure is also very high. Reported grade III-IV complications occur in 15-66% of the patients, divided into three major categories: digestive fistulas, pulmonary and hematologic complications. Reoperation rate vary between 7 and 24%<sup>9</sup>.

SC-HIPEC protocol was initiated 13 years ago at the Geneva University Hospitals. During this period, 60 surgical explorations for PC were performed (37 in the last 3 years, figure 2). Complete cytoreduction was estimated impossible in 9 patients. Median age of the 51 resected patients (34 F, 17 M), was 52 (17-65). Primary cancers were pseudomyxomas in 31%, colorectal in 23%, ovarian in 25%, gastric in 15% and mesotheliomas in 6%.

Overall postoperative morbidity (grade I-IV) according to the Clavien classification<sup>13</sup> was 69%; severe morbidity (grade III-IV) was 39%; reoperation was warranted in 22%; perioperative mortality (D60) was 2% (n=1); median hospital stay was 22 days (12-84).

Median follow-up was 13.5 months (1-196), with an actuarial five-year survival rate of 57%. Ten patients died of disease; 41 patients are still alive, from which 85% (35/41) are presently without signs of recurrence.

## Conclusions

Our results, as well as those of achieved by more experienced teams in the field of surgical therapy of PC, show that, in very selected patients, SC-HIPEC can have a strong impact on the prognosis of PC. In this context, the high observed morbidity appears acceptable. The most significant determinants of success of this procedure are the completeness of surgical cytoreduction and a careful patient selection. SC-HIPEC has a very promising future in specialized centers.

