Peritoneal carcinomatosis of colorectal origin: is it really an end-stage disease?

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Received: 15 July 2013 / Accepted: 18 August 2013 / Published online: 6 September 2013
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Peritoneal carcinomatosis (PC) is no longer considered as a systemic disease. There is mounting evidence for a local spread theory [1]. Peritoneal tumor implantation occurs due to multiple mechanisms including serosal invasion, leakage of malignant cells through the lymphatics, or as a result of imprudent dissection [2].

The exact extent of the PC can be determined precisely only during surgery. The peritoneal cancer index (PCI, Washington Cancer Institute) is usually used to quantify PC. This explains why the estimation of the extent of PC was sub-optimal in historical series where patients were treated systematically without formal staging [3].

In the most recent revision of the TNM staging system [4], metastatic colorectal cancer (CRC) at initial diagnosis is sub-classified into stage IVA or IVB disease according to the number or site of metastases. In this system, PC is sub-classified into stage IVB, whereas other metastases to a sole organ such as liver or lung are sub-classified into stage IVA, which is considered to indicate better survival. The new TNM classification system was proposed and validated before publication by the American Joint Committee on Cancer (AJCC) Hindgut Taskforce based on a large population-based study, surveillance, epidemiology, and end results (SEER) of patients with CRC treated between 1994 and 2005 in the USA [5, 6].

The major historical series (i.e., before the era of newer chemotherapy, cytoreductive surgery [CRS], and heated

intraperitoneal chemotherapy, [HIPEC]) suggested a poor prognosis with a median survival around 6 months and absolutely no long-term survivors [6–8].

However, for almost a decade now, the prognosis of patients with PC of colorectal origin has been improving. This is mainly due to two factors, the use of oxaliplatin-based chemotherapy [9] and the combination of CRS with HIPEC as a possible treatment modality [10].

These findings raise the question of whether sub-classification into stage IVB is still appropriate and clinically relevant.

Ishida et al. [11] conducted a retrospective study in order to investigate the overall survival in metastatic CRC patients based on the sites of metastasis in the era of modern chemotherapy. The authors found that patients with isolated PC had a median survival of 36.6 months, as compared to a median survival of 32.5 months ($p = 0.48$) for patients in the IVA group. These figures were significantly higher than those of patients with distant metastases with or without PC [14.7 months ($p = 0.07$) and 12.9 months ($p < 0.01$), respectively]. The authors recommend including patients with isolated PC in the IVA group rather than those in the IVB group.

Only about a third of all patients with PC would be suitable for an aggressive, multimodal therapy, combining CRS with HIPEC and systemic chemotherapy. In order to improve the prognosis, complete resection of the entire macroscopically visible tumor mass is mandatory. Remaining microscopic tumor cells should be eradicated immediately after resection with HIPEC. With such an approach, median survival has been reported to reach more than 30 months, with 3- or 5-year survival rates of more than 30 %, in some series [12]. Patient selection is, however, crucial. A positron emission tomography (PET) scan is a valuable tool for selecting patients with isolated PC

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[13]. It is effective in detecting PC and has the potential to improve clinical diagnosis when coupled with an understanding of the pathways of flow for ascitic fluid and peritoneal seeding.

The efficacy of CRS–HIPEC for patients with PC is to be weighed against its inherent high morbidity and mortality rates. Mortality rates up to 19 % and morbidity rates up to 55 % have been, respectively, reported with some CRS–HIPEC regimens [14]. However, the mortality rate in centers where more than 100 patients have already been treated is less than 3 % [15]. Median survival following complete resection (R0) of all microscopic diseases ranged from 18 to 39 months [16]. In the same R0 setting, 5-year survival ranged from 20 to 54 % [16]. On the other hand, when more than 5-mm residual disease was left behind, median survival oscillated between 5 and 12 months, with no 5-year survivors, figures mimicking those reported in historical series [16]. Multidisciplinary tumor board agreement is needed to pursue this aggressive combined treatment strategy.

The available systematic studies of postoperative quality of life show—depending on the extent of the surgery and the rate of peri- and postoperative complications—a deterioration in quality of life in the first few weeks following surgery. However, most patients achieve at least the same level of quality of life as before the operation during the few months following surgery [16].

In the absence of prospective studies, the analysis of the French register shows that adjuvant systemic chemotherapy correlates with a better prognosis for the patient, with a median survival of 34 months and a 5-year survival of over 30 % [12].

Even if long-term survival has been achieved with aggressive treatment of patients with PC, patients with this disease have a dismal prognosis, with only less than 30 % being candidates for possible long-term survival. Our team believes that adjuvant HIPEC could theoretically reduce the risk of PC in selected patients undergoing surgery with curative intent for CRC. In 2005, we proposed a pilot study to evaluate the feasibility, safety, and short-term outcome of laparoscopic adjuvant HIPEC in selected patients after complete resection of locally advanced colorectal or gastric cancer. The preliminary results of this study have already been published [17].

Mid-term results are yet to be published. However, the overall follow-up period of the patients who survived more than 2 years was 30.5 months (range 24–49 months). Only 12 % of these high-risk patients developed PC, while the theoretical risk could be up to 55 % [18, 19].

In summary, although the pathophysiology of PC is different from that of liver metastases, both diseases have roughly comparable outcomes. In selected cases, long-term survival could be achieved utilizing combined, aggressive

medico-surgical regimens. Moreover, in patients at high risk of developing PC, adjuvant HIPEC could be of some interest in the future. Further large-scale evaluation is recommended.

Conflict of interest None.

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