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## EDITORIAL

# Peritoneal carcinomatosis is multifaceted, treatment requires expertise and collaboration with other health care personnel: New avenues of research are open



Management of peritoneal metastases, or carcinomatosis, has evolved very quickly over the last years. While this is also true for many diseases, real progress for advanced malignant disease has been and remains, rather rare. Instead of constituting a quasi-death sentence as it did only twenty or so years ago, peritoneal metastatic disease now has real solutions that we can propose to selected patients. Of note, the particularity of these solutions is that they are not to be conveyed by one practitioner alone, as, for instance, is the case for liver metastases. Expertise and skills must be conjugated. Current progress for ovarian carcinomatosis has recently resounded in the *Journal of Visceral Surgery* [1]. Effectively, following the results of randomized trials, it is accepted today that:

- when amenable to complete surgical excision, ovarian carcinomatosis should undergo surgery after inductive chemotherapy, a procedure that, while decreasing the sequels of surgery, has not changed survival;
- routine lymphadenectomy for stage 4 disease does not improve survival and therefore can be abandoned, and;
- performance of Hyperthermic Intra-peritoneal Chemotherapy (HIPEC) after complete cytoreductive surgery increases patient survival [1].

The change is major and requires that the recommendations of French national and learned societies be revisited, and in particular, that HIPEC be proposed as part of the therapeutic armamentarium [2]. The recent Dutch study published on oxiplatin-based HIPEC for ovarian carcinomatosis has shown a survival gain of one year [3]! A French comparative study also found that HIPEC was associated with a one-year gain in survival when used for gastric carcinomatosis [4]. With only one prospective Japanese study having been published previously, this study represents the highest level of evidence available today. So, yes, complete cytoreductive surgery and HIPEC are now recommended for gastric carcinomatosis if the disease is limited!

But all is not that simple and progress has been chaotic; the best therapeutic solutions are difficult to define, different for each type and stage of carcinomatosis. This is what you will read in the last issues of *Visceral Surgery* [5–7]. The first of three articles on the topic is the result of a reflection of a large panel of surgeons, oncologists, gastro-enterologists, pathologists and radiologists. Collaboration between specialists is essential, in order to keep pace with current knowledge. While the French PRODIGE study has not yet been published, these practitioners have set new benchmarks when they presented their results at the American Society of Clinical Oncology (ASCO) meeting in 2018 [8]. This article proposed to revise the fundamentals of management of patients with carcinomatosis of colonic origin, because the current policy in France, associating hyperthermia and high dose oxaliplatin, was found to be not very effective or the effect was not strong enough while at the same time, being too toxic [5]. But the good news is that survival longer than 40 months is possible without HIPEC for certain patients with carcinomatosis of colonic origin. This also opens the possibility of proposing cytoreductive surgery to patients who are older or have other serious co-morbidities that previously would not have been possible because the “mandatory” HIPEC component of this management plan would be too risky. Currently, patients over 75 years should not be routinely denied surgery. If all carcinomatosis can be removed, you can expect to improve patient survival. Of note, collaboration with a geriatrician is important to curtail surgical morbidity [5].

Some authors, and in particular our neighbors from Germany, have made strong arguments in favor of cytoreductive surgery associated with HIPEC, including for patients with concomitant liver metastases [6]. Here, we can only commend the expertise of our German colleagues who have perfectly mastered the postoperative follow-through and thus have reported a median survival of 22 months for patients with multiple gastro-intestinal metastatic disease. Such series of combined liver and peritoneal surgery attest to the possibility of treatment with curative intent when more than one organ is involved. Here again, collaboration with pathologists to finetune strict selection criteria – that is avoiding patients with mutated BRAF tumors or tumors with high proportions of signet cell carcinoma – is as important as collaboration with radiologists and oncologists. Finding the particular solution adapted to each patient, and associating different strategies are essential. While simple liver surgery can be proposed for a subcapsular metastasis, the indication for a class 2 hepatectomy is quite another story. Should intra-operative radio-ablation be privileged? Or is two-stage surgery the solution? And if so, which should be addressed first, the liver or the peritoneal metastatic location? One must not forget that correctly performed, chemotherapy alone should provide a survival of more than 12 months, and therefore the high morbidity associated with this high-risk surgery should be weighed in carefully. And lastly, maybe the best therapeutic approach would be a collaboration between a liver and a peritoneal surgeon, and in this setting, part of the liver surgery could be laparoscopic while the peritoneal component would be via laparotomy.

When cytoreductive surgery is not indicated, a new solution, such as pressurized intra-peritoneal aerosol chemotherapy (PIPAC) is one of the most recent innovations for surgical treatment of carcinomatosis. This modality consists of an aerosol of vaporized chemotherapy administered during laparoscopy. It is easily understandable that there are safety concerns for the patient as well as for the health care personnel. This is one of the major constraints of this technique, which is why the thirty article of last issues in the Journal details these constraints and the collaboration that is necessary between pharmacists, the biomedical department and all the personnel working in the operating room [7]. This article from our colleagues in Strasbourg should set the scene for other teams to embrace this technique, currently performed worldwide more than 3000 times since 2019, without fear. Effectively, it seems possible to perform PIPAC in operating rooms without laminar air flow protection, which was recommended initially only a few years ago. Again, progress has been made and this technique is destined for wider diffusion. Not less than four hospital clinical research projects are planned to start within the next few months to test the place of PIPAC in the treatment of gastric, colonic, ovarian carcinomatosis or peritoneal mesothelioma.

Therefore, collaborate to offer each patient with peritoneal metastasis a solution adapted to the needs, irrespective of the degree of cancer involvement, collaborate to learn how to treat these patients from others, to learn the art of surgery of the peritoneum which continues to become more and more complex, collaborate to ask expert teams for advice, with today, new possibilities of intra-peritoneal chemotherapy and new hope for patients.

## Disclosure of interest

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