A Comparative Study of Complete Cytoreductive Surgery Plus Intraperitoneal Chemotherapy to Treat Peritoneal Dissemination From Colon, Rectum, Small Bowel, and Nonpseudomyxoma Appendix

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Objective: To report a large number of patients with peritoneal carcinomatosis (PC) treated with complete cytoreductive (CCR-0) plus intraperitoneal chemotherapy, and to compare the results according to the origin of the primary: colon, rectum, small bowel, and appendix (excluding peritoneal pseudomyxoma).

Patients and Methods: Among 615 patients treated for PC originating from these 4 types of primaries in 23 French centers, 440 were retrospectively selected as having undergone complete cytoreductive surgery and with complete data retrieval. Primary sites were: colon (n = 341), rectum (n = 27), appendix (n = 41), and small bowel (n = 31).

Results: Postoperative mortality and morbidity (3.9% and 31%, respectively) did not differ according to the origin of the primary tumor. The mean follow-up was 60 months. The 5-year overall survival rates were not statistically different for the colon (29.7%), rectum (37.9%), nor the small bowel (33.8%), but was higher ($P = 0.01$) for appendix adenocarcinoma (63.2%). The multivariate analysis of prognostic factors singled out the extent of peritoneal seeding ($P < 0.0001$), positive lymph nodes ($P = 0.001$), and adjuvant systemic chemotherapy ($P = 0.002$), whereas the origin of the tumor was borderline ($P = 0.06$) in favor of appendix tumors.

Conclusion: Cytoreductive surgery plus intraperitoneal chemotherapy yields satisfying and similar survival results in the treatment of PC from colon, rectum, and small bowel adenocarcinomas. Results were better for appendix adenocarcinoma. When feasible, this combined approach should become the gold standard treatment of PC.

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Peritoneal dissemination or "carcinomatosis" from digestive carcinoma is a proliferative event which concerns 30% to 40% of the patients.[1,2] Natural history studies show that peritoneal carcinomatosis (PC) is uniformly fatal with median survival ranging from 6 to 24 months.[3,4] For more than a decade, a handful of centers have pursued aggressive cytoreductive surgery combined with intraperitoneal chemotherapy (IPC), initially without, and after with hyperthermia, as an alternative approach to this disease. Five-year survival rates range from 19% to 48% for PC from colon carcinoma[5–8] and from 52% to 96% for PC from peritoneal pseudomyxomas.[9–12] This new approach applied to primary colon carcinoma and peritoneal pseudomyxoma has therefore yielded relatively concordant results. However, there are virtually no data in the literature on PC originating from the rectum, small bowel or from appendiceal tumors (excluding *pseudomyxoma peritonei*), and no study has presented a comparison between these different but rather close primaries. In 2008, a French multicentric study from 23 centers[7] allowed us to collect data from numerous patients treated with the combined approach, to obtain survival results and to compare these results according to the origins of the primary tumors.

The purpose of our study was to analyze the results obtained in a large multicentric cohort of patients maximally treated with complete cytoreductive surgery (CCR-0 = no remaining macroscopic tumor seeding) and IPC, and to compare them according to the site of origin (colon, rectum, small bowel, or appendix).

PATIENTS AND METHODS

Patient Population

In 2008, the annual report of the Association Française de Chirurgie was devoted to the treatment of PC with cytoreductive surgery and intraperitoneal chemotherapy. This allowed the retrospective retrieval of data concerning 1290 patients treated in 23 centers between 1989 and 2007. Among them, 615 patients had presented with PC originating from the colon (n = 496), appendix (n = 50), small bowel (n = 45), and rectum (n = 37). Among these 615 cases, patients were selected for this study based on the following 3 criteria: (1) The presence of PC originating from one of these 4 sites and confirmed by a pathologic examination at the time of cytoreductive surgery, (2) CCR-0 had been carried out with no visible remaining tumor nodules, and (3) a complete data form without missing information. Exclusion criteria were the presence of extra-abdominal metastases and peritoneal pseudomyxomas (301 cases of pseudomyxomas were similarly treated by the 23 centers during the same period). The rectal site of the tumor was defined as tumor with an inferior bound sited at less than 15 cm from the anal margin. Appendiceal adenocarcinoma without pseudomyxoma was defined both macroscopically (absence of a mucinous component) and microscopically (no extracellular mucus).

Data Forms

Standardized clinical data on consecutive patients from each of the 23 institutions were entered into a central database. A standard data form was created to retrieve information on the primary tumor, information on the status of the patient before submission to the combined procedure, and previous treatment with systemic chemotherapy. A mailed hard copy of these deidentified data forms was sent to the data center. The extent of PC was assessed by intraop-

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