Patients with Nonovarian Peritoneal Carcinomatosis Achieve Long-Term Survival

A recent retrospective study has shown that long-term survival can be achieved in some patients with peritoneal carcinomatosis (PC) from nonovarian malignancies by using cytoreductive surgery and perioperative intraperitoneal chemotherapy (PIC) (Cancer [published online ahead of print August 24, 2010] doi: 10.1002/cncr.25356).

Olivier Glehen, MD, PhD, professor of surgical oncology at South Lyon University Hospital in Lyon, France, and colleagues conducted a review of 1290 patients with PC from 25 French-speaking institutions who had undergone 1344 procedures combining cytoreductive surgery and PIC from 1987 to 2007. Patients with any extra-abdominal metastases were excluded from this study. All patients received PIC, comprised of either hyperthermic intraperitoneal chemotherapy (HIPEC), early postoperative intraperitoneal chemotherapy, or both administered within 7 days of surgery, although most patients (n = 1106) underwent HIPEC.

Numerous underlying malignancies were included, but colorectal cancer comprised the bulk at 40%, followed by pseudomyxoma peritonei (23.3%), gastric cancer (12.3%), peritoneal mesothelioma (6.8%), and appendiceal adenocarcinoma (3.9%), among others.

“The best candidates for this approach are patients younger than 70 years old, with good performance status, no extra-abdominal disease, and with carcinomatosis that can be completely removed by cytoreductive surgery,” Dr. Glehen says.

The HIPEC Procedure

The HIPEC procedures were all performed intraoperatively, although there was variation in the exposure techniques (open vs closed abdomen), duration of exposure to chemotherapy, the chemotherapy drugs used, type of perfusate, flow rates, and intraperitoneal temperatures.

“Many regimens of intraperitoneal chemotherapy may be used and have been validated by prior phase 2 studies such as mitomycin C, oxaliplatin, irinotecan, doxorubicin, and cisplatin,” Dr. Glehen says. “The use of targeted therapy by the intraperitoneal route is still experimental and bevaxizumab is currently under study at our institution. Further, open and closed HIPEC techniques seem to give equivalent results.”

The authors note, however, that the impact of different PIC techniques, including the drugs used, could not be assessed in the current study due to marked variation among institutions. Approximately 35% of patients received subsequent systemic adjuvant chemotherapy based on their prognostic features.

Paul Sugarbaker, MD, director of the Peritoneal Surface Malignancy Program at Washington Hospital Center, notes that, in general, there is variation in the length and complexity of the surgery. “If there is minimal disease such as a perforated colon cancer or a gastric cancer with only a few peritoneal seedlings, the time spent in the operating room would be approximately 6 hours,” he says. “This would be 4.5 hours for surgery and 90 minutes for the HIPEC procedure. In those patients who have a large extent of disease, the procedure can take up to 12 hours. In the last few years, the referrals have been much earlier so the length of the surgery is, fortunately, greatly reduced.”

Postoperative Complications, Mortality, and Survival

The postoperative mortality rate was 4.1%, and 33.6% of patients experienced grade 3 or 4 complications (most frequently neutropenia, digestive fistula, or pneumonia). Logistic multiple regression analysis was used to identify factors independently associated with morbidity, mortality, and survival. Increasing patient age, greater extent of...
carcinomatosis, and shorter duration of experience with cytoreductive surgery of the treating institution were independently associated with significantly increased morbidity and mortality rates.

The median follow-up was 45.3 months with overall 1-year, 3-year, and 5-year survival rates of 77%, 49%, and 37% respectively. Researchers reported an overall median survival of 34 months (30 months for colorectal cancer patients, not reached in patients with pseudomyxoma peritonei, 9 months for gastric cancer patients, 41 months in mesothelioma patients, and 77 months for patients with appendiceal adenocarcinoma).

On multivariate analysis, the independent prognostic factors that significantly affected survival rates in addition to the effects of treatment center included etiology of PC, extent of carcinomatosis, completeness of cytoreduction, and the presence of disease in the lymph nodes. Survival also was found to have significantly improved over the study period from 1989 to 2004.

“Treatment of carcinomatosis is very similar to treating any malignancy,” Dr Sugarbaker says. “The earlier the treatment and the smaller the extent of disease, the better the result. Also, as in other malignancies, the aggressive nature of the disease often determines the outcome. The low-grade diseases such as pseudomyxoma peritonei had the best outcomes. Additionally, there are some patients with peritoneal mesothelioma that had low biological aggressiveness. The outcome in these patients is extremely good and cure is expected.”

The authors write that institutional experience significantly affected overall survival, morbidity, and mortality, most likely because of better patient selection, surgical expertise, and postoperative management. They note that this finding is in keeping with reports from other authors showing decreasing mortality rates with increasing experience, a point with which Dr. Sugarbaker strongly agrees.

Dr. Sugarbaker says he is concerned that widespread access to centers with experienced multidisciplinary PC teams is lacking, adding that groups that do well are those that use the multidisciplinary team approach. “An oncologic team of radiologists, oncologists, and surgeons [is] necessary in order to consistently manage patients in an optimal manner…,” he says. “Unfortunately, many medical oncologists do not realize that data regarding the treatment of peritoneal carcinomatosis with systemic chemotherapy [are] completely lacking. The only treatment that has clinical science support is cytoreductive surgery plus HIPEC.”

Dr. Sugarbaker also points to websites, such as http://www.pmppals.org, http://www.pmtparent.org, and http://www.curemeso.org, where patients can find centers that perform cytoreductive surgery and HIPEC. He says his impression is that there have been recent increases in referrals to these centers, which seem to be mostly patient-driven.

**Standard of Care?**

Perhaps the most important message from this study, according to Dr. Glehen, is that curative treatment of PC (including cytoreductive surgery and HIPEC) needs to be considered at the time of diagnosis for all patients with appropriate general status and carcinomatosis that may be completely resected.

Dr. Glehen notes that 2 other registries (with more than 500 patients each) demonstrated 5-year survival rates of more than 25% to 30% with combined cytoreductive surgery and intraperitoneal chemotherapy. “This kind of result has never [been] obtained by systemic chemotherapy alone,” he says. “New guidelines for oncologists and general surgeons should be developed and extensively reported because of these results that should change the therapeutic management of this disease.”

Dr. Sugarbaker agrees that PC should not necessarily be considered a terminal event and that cytoreductive surgery and HIPEC should be incorporated into guidelines. “Much work needs to be done with carcinomatosis,” he says. “It has been called the ‘final frontier’ in the management of the cancer patient. The French group deserves great credit in standardizing the procedures throughout France, continuing important clinical and pharmacologic research, and making cytoreductive surgery plus HIPEC a standard of care. It is also a standard of care for colorectal cancer in the Netherlands, where a large amount of clinical research has been performed at the Netherlands Cancer Institute.”

**Note:** The name of this section has been changed from “News & Views” to “Perspectives: Research in Context.” It continues to provide the context for major developments in cancer prevention, detection, and treatment.