Patient Selection for Cytoreductive Surgery

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KEYWORDS

• Prognostic factors • Predicting • Patient selection • Outcomes • HIPEC
• Cytoreduction

KEY POINTS

- Clinical factors, such as age, comorbidities, smoking, and functional and nutritional status, are important to minimize morbidity from cytoreduction (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC).
- Simplified Preoperative Assessment for Appendix Tumor (SPAAT) score is helpful in determining expectations from CRS and HIPEC for well-differentiated mucinous appendiceal adenocarcinoma.
- Response to neoadjuvant chemotherapy and extent and volume of distribution of disease on laparoscopy are important for selecting patients with high-grade disease for CRS and HIPEC.
- Histology and various measures of proliferation (Ki-67, mitotic rate, and SUV-max on PET) are important in selecting patients with peritoneal mesothelioma for CRS and HIPEC.
- PCI of greater than 20 for high-grade appendiceal, greater than 17 to 20 for colorectal cancer, and greater than 7 for gastric cancer are relative contraindications for CRS and HIPEC.

CYTOREDUCTION FOR PERITONEAL MALIGNANCIES

"In the world of surgical oncology; biology is King; selection of cases is Queen, and the technical details of surgical procedures are princes and princesses of the realm who frequently try to overthrow the powerful forces of the King and Queen, usually to no long-term avail, although with some temporary apparent victories." This insight first shared by Blake Cady, MD more than 20 years ago remains just as true today. Nowhere is this more relevant than the group of cancers with a biologic predisposition

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for peritoneal dissemination collectively referred to as the peritoneal malignancies. The peritoneal malignancies span the biologic spectrum of aggressiveness from the indolent growth pattern and superficial nature of well-differentiated mucinous appendiceal adenocarcinoma to the rapidly growing and invasive nature of poorly differentiated signet ring cell adenocarcinomas of the appendix, colon, and stomach. Likewise, the peritoneum is a unique site of metastasis comprising 13 distinct abdominopelvic regions in the peritoneal carcinomatosis index (PCI) described by Sugarbaker. Each of these regions has its own associated challenges to evaluation and resection. The volume and distribution of disease within the peritoneal cavity are incorporated in the PCI and are consistently identified as an important prognostic factor for recurrence and survival. As the PCI increases the likelihood of complete cytoreduction and long-term survival decrease; however, there remains patients with extensive disease who are able to achieve a complete cytoreduction and improved survival. One of the limitations of the PCI is that it assigns points equally among the 13 abdominopelvic regions according to volume of disease and does not stratify points according to the difficulty of resection or presence of critical structures within each abdominopelvic region. This is a critical shortcoming because involvement of the upper and lower jejunum and the upper ileum are associated with a particularly worse outcome because of the inherent difficulties with removing all the disease in this location. In contrast, involvement of the left flank, left lower quadrant, and the right flank are associated with improved outcomes because of the relative lack of critical structures in these regions. An understanding of the biology, distribution, and volume of disease is critical to appropriately selecting patients for aggressive treatment with the goal of long-term survival.

Historically there has been little understanding of the tumor biology of peritoneal malignancies, which has until recently prevented a thoughtful approach to peritoneal metastasectomy. In 1998, the first randomized controlled trial for peritoneal carcinomatosis from colorectal and appendiceal adenocarcinoma began accrual. This trial randomized patients to the current standard of care at that time: systemic 5-FU chemotherapy alone or cytoreduction (cytoreductive surgery [CRS]) and hyperthermic intraperitoneal chemotherapy (HIPEC) followed by systemic 5-FU chemotherapy. Because of the uncommon nature of peritoneal carcinomatosis and the lack of any known selection factors there were few exclusion criteria. Both first presentation and recurrences were included. Abdominal computed tomography (CT) scan and chest radiograph were the only required staging imaging. The only clinical criteria were age less than 71 and normal hematologic, renal, and liver laboratory parameters. There were no stipulations regarding the volume and distribution of peritoneal disease. Despite the unselected nature of this study and the high perioperative mortality (8% in this study), which was a result of the steep learning curve associated with CRS and HIPEC and the advanced nature of the peritoneal disease studied, the trial demonstrated a doubling of survival compared with the control arm (22.3 months vs 12.6 months median overall survival [OS]). It was only in subset analysis of prognostic factors in the CRS and HIPEC arm that it was evident that patients with cancer deposits in six or seven of the seven possible regions in the Dutch Simplified Peritoneal Cancer Index do poorly, in respect to direct postoperative complications and long-term survival. In fact, the authors attributed 80% of all grade 4 toxicity and all treatment-related deaths to the patients with involvement of six or seven abdominal regions. Similarly, these are the same patients in whom a complete cytoreduction was unable to be obtained and the survival was similar for these patients whether they were treated with systemic chemotherapy alone or cytoreduction and HIPEC. These patients clearly did not benefit from cytoreduction. In contrast, the patients