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EDITORIAL – GASTROINTESTINAL ONCOLOGY

# Moving Fast and Moving Slow

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The Ninth International Symposium on Regional Therapies at Steamboat Springs, Colorado brought forth some of the finest research occurring in the management of advanced malignancies. We are pleased to present some of this work in the *Annals of Surgical Oncology*. Although it is difficult to do justice to the perseverance of the teams, the investigation of the scientists, and the sacrifices of our patients in a few pages, we hope to provide you with a snapshot of a rapidly changing field. Delivering cytotoxic therapy in a proinflammatory healing state after an operation requires the development of a precise framework—the hallmark of regional therapies. Advancement of care has required rapid intuitive thinking and development of surgical concepts that have allowed us to apply selective regional therapies to patients more widely than ever before. It is estimated that more than 1,300 cytoreductive procedures and hyperthermic intraperitoneal chemotherapy (HIPEC) procedures were performed in the United States in 2012, and the numbers are increasing. The rapid pace of these advances has brought with it careful investigation of the aspects of care, focusing on oncological outcomes, safety, and patient-centered metrics. These developments have been associated with the growth of new centers both locally and internationally, thereby improving access to care.

The articles from the Symposium explore the application of aggressive surgical resection in the setting of chemoperfusion. Randle et al. studied 108 patients from a prospective database of 1,067 patients who underwent hepatic resection concomitantly with cytoreductive surgery (CRS) and HIPEC.[1] After establishing two groups—one with patients who underwent surface resection alone versus the other in which the patients were subjected to parenchymal resection—they found that the perioperative morbidity and mortality rates were similar. The overall survival for the group with colorectal cancer and peritoneal and hepatic metastases was 21.2 months. In a separate analysis, the authors examined 89 patients with diaphragmatic involvement who underwent CRS and HIPEC. In contrast to their previous report, the authors found that morbidity associated with the surgery was seen at a significantly higher rate among those undergoing diaphragmatic resection, especially in patients who required resection of fewer than five organs.[2]

Distribution of peritoneal disease often leads to involvement of the splenic hilum, necessitating distal pancreatectomy. Doud et al. reported on 63 patients who underwent distal pancreatectomy with a 30 % major morbidity rate and a significantly longer hospital stay than those that did not.[3] Further adding to the evidence regarding the risks of a distal pancreatectomy, Downs-Canner et al. compared patients undergoing distal pancreatectomy with and without intraperitoneal chemotherapy.[4] They found that although the number of patients developing pancreatic fistulas was similar the morbidity associated with the fistulas was greater. In addition, the development of complications came at an oncological cost. Patients with fistulas had earlier recurrence of their disease. Nunez et al. looked at another surgical issue: whether abdominal wall resection and reconstruction carry a higher postoperative morbidity rate.[5] Often, port-site excision or reexcision of the abdominal wall is necessary for oncological cytoreduction. The morbidity rate was 33 % in those undergoing port-site excisions, 21 % in those undergoing primary fascial closure, and 41 % in those undergoing reconstructive surgery.



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Interpretation of these reports requires understanding the nature of peritoneal disease. A greater tumor burden likely indicates more aggressive disease, which necessitates more CRS. Determining the effect of intraperitoneal chemotherapy on complications is difficult. Bartlett and colleagues examined the NSQIP database to identify 188 patients undergoing colorectal resection with intraperitoneal chemotherapy and compared them to a propensity matched cohort.[6] They found that morbidity and mortality were not different in the two groups.

The unifying feature of all the reports herein was a carefully selected cohort of patients who were evaluated and treated at a center experienced in peritoneal surface malignancies. Experience might play a role in considering patients for CRS, especially iterative surgery. Polanco et al. analyzed cases at a high-volume center and found that the learning curve for treating appendiceal tumors and mesothelioma required 180 cases for an end result of minimizing morbidity and 90 cases for oncological safety.[7] These data are supported by the report from the Washington Hospital Center reports on patients with mesothelioma who underwent iterative CRS with acceptable morbidity and improved survival outcomes.[8] When defining experience, however, it is critical to evaluate the published evidence and then synthesize its meaning. Helm et al. present a systematic review of all reports of patients undergoing CRS+HIPEC for malignant mesothelioma.[9] The report helps identify chemotherapeutic agents that are more clearly associated with better survival benefit than others.

Prediction of successful outcomes is desirable before undertaking any invasive procedure. The next set of articles examine methods for defining success and then examine the tools for predicting success. Quality of life (QOL) is an important metric of success. Jiang et al. validate a novel tool to measure QOL in patients undergoing isolated limb infusion procedures.[10] Three articles (by Tohme et al.,[11] Low et al.,[12] and Baumgartner et al..[13]) are important as they demonstrate the advances being made in the field to better predict our failures. The first article looks at a simple biomarker to predict survival after radioembolization for metastatic colon cancer using neutrophil and lymphocyte ratios.[11] The second looks at the utility of novel imaging with magnetic resonance technology to predict more accurately the peritoneal burden of disease.[12] The third looks at predictors of progression after CRS+HIPEC and found that nodal disease was likely the most significant factor. Innovative approaches to the management of patients with peritoneal disease are highlighted further. Laparoscopic evacuation of ascites for palliation is reported on 10 patients by Kelly et al. who demonstrate durable symptom control with minimal morbidity.[14] The innovative management of pediatric malignancies with CRS+HIPEC was pioneered by Hayes-Jordan and colleagues, who report successful outcomes for the first 50 cases.[15] Innovative approaches for setting up a national center of excellence in Colombia are demonstrated by Arias and colleagues.[16] It is an important example of setting up a world class facility in a limited-resource setting. Managing resources might be the largest challenge we will face in the coming years. Squires et al. take on the controversial task of reporting on the financial burden of CRS and HIPEC in a hospital system, especially where a third-payer system is in place.[17] Their conclusions support a profitable procedure in private-payer settings with losses for the publicly supported insurance plans. This disparity was echoed by Tabrizian and colleagues, who found that regional therapies were preferentially applied to those with private insurance likely because of the lack of coverage by the other plans.[18]

This humbling reality is where we begin—where financial realties can overshadow science and patient care. What we have seen is an unprecedented number of investigators refining a technique steeped in tradition and then innovating and studying better ways to improve outcomes. What we need is continued investigation of empirical ideas, development of novel cost-effective therapies with minimal morbidity, and a collaborative approach to advancing the field.

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