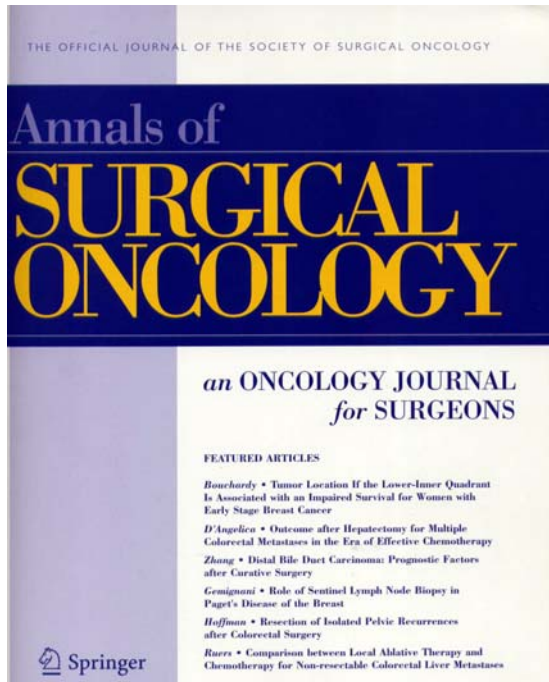


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Impact of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemo-therapy on Systemic Toxicity

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Introduction: The purpose of this study was to analyze the postoperative systemic toxicity and procedure-related mortality (PRM) of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in the treatment of peritoneal surface malignancies (PSMs). **Patients and methods:** A total of 242 (84 males/158 females) patients with PSM underwent 247 consecutive procedures. The mean age was 52 years (range 22–79). CRS was performed using peritonectomy procedures. The HIPEC technique through the closed abdomen was conducted with cisplatin (CDDP 25 mg/m²/l of

perfusate)+mitomycin C (MMC 3.3 mg/m²/l perfusate) or CDDP (43 mg/l perfusate)+doxorubicin (Dx 15.25 mg/l perfusate) at 42.5°C. These dosages were reduced by 30% when the patient had received systemic chemotherapy before the CRS+HIPEC. Systemic toxicities were graded according to the NCI CTCAE v3 criteria. **Results:** G3-5 systemic toxicity rate was 11.7 % and adverse events were bone marrow suppression, 13; nephrotoxicity, 14; neutropenic infection, 2 and pulmonary toxicity, 1. Independent risk factors for G3-5 systemic toxicity after multivariate analysis were a dose of CDDP for HIPEC of 240 mg or more (OR 2.78, CI 95% 1.20–6.45) and CDDP+Dx schedule for HIPEC (OR 2.36, CI 95% 1.02–5.45). PRM was 1.2%. **Conclusions:** CRS+HIPEC presented acceptable systemic toxicity and PRM rates. Independent risk factors for systemic toxicity were the CDDP+Dx schedule and CDDP dose for HIPEC.

Palliative Resection of Colorectal Cancer: Does It Prolong Survival?

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Background: It is still a matter of debate as to whether resective surgery of the primary tumor may prolong the survival of patients affected by incurable colorectal cancer (CRC). The main goal of this retrospective study, carried out on patients not undergoing any therapy other than surgery, was to quantify the benefit of primary tumor removal in patients with differently presenting incurable CRC. **Methods:** One hundred and thirty consecutive patients were operated on for incurable CRC (83 undergoing resective and 47 non-resective procedures). With the purpose of comparing homogenous populations and of identifying patients who may benefit from primary tumor resection, the patients were classified according to classes of disease, based on the "metastatic pattern" and the "resectability of primary tumor." **Results:** In patients with "resectable" primary tumors, resective procedures are associated with longer median survival than after non-resective ones (9 months vs 3). Only patients with distant spread without neoplastic ascites/carcinosis benefit from primary tumor removal (median survival: 9 months vs 3). Morbidity and mortality of resective procedures is not significantly different from that of non-resective surgery, either in the population studied or in any of the groups considered.

Conclusions: Palliative resection of primary CRC should be pursued in patients with unresectable distant metastasis (without carcinomatosis), and, intraoperatively, whenever the primary tumor is technically resectable.

Update of Carcinoembryonic Antigen Radioimmunotherapy with ¹³¹I-Labetuzumab After Salvage Resection of Colorectal Liver Metastases: Comparison of Outcome to a Contemporaneous Control Group.

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Background: We tested whether adjuvant radioimmunotherapy (RAIT) given after R0 resection of liver metastases (LM) of colorectal cancer is safe and can improve survival. Resection of LM from colorectal cancer is the standard of care in this setting, yet two thirds will eventually relapse, and adjuvant systemic chemotherapy has failed to improve survival. **Methods:** Twenty-three patients who underwent R0 resection for LM of colorectal cancer received a dose of 40 to 60 mCi/m², ¹³¹I-labetuzumab, a humanized monoclonal antibody against carcinoembryonic antigen. Safety (n = 23), disease-free survival, and overall survival (n = 19) were analyzed, and efficacy was then compared retrospectively with a similar contemporaneous group of control patients (n = 19) treated at the same institution during the same time period but without RAIT. **Results:** At a median follow-up of 91 months (95% confidence interval [CI], 68.0 months to infinity), the median overall survival for RAIT patients was 58.0 months (95% CI, 55.0 months to infinity), versus 31.0 months (95% CI, 26.0 months to infinity) at a 51-month median follow-up for the controls (P = .032). The median disease-free survival for RAIT patients was 18.0 months (95% CI, 11.0–31.0 months), versus 12.0 months (95% CI, 6.5–27.0 months) for the controls (P = .565). Corresponding survival rates (Kaplan-Meier analyses) were estimated to be 94.7% at 1 year, 78.9% at 2 years, 68.4% at 3 years, and 42.1% at 5 years with RAIT and 94.7%, 68.4%, 36.8%, and 15.8%, respectively, for the controls. RAIT was beneficial independently of bilobar involvement, size and number of LM, or resection margins. Transient myelosuppression was the principal adverse effect. **Conclusions:** This first evidence of a promising survival advantage of adjuvant RAIT after long-term follow-up of colorectal cancer patients given salvage resection of LM warrants confirmation in a prospective randomized trial.

The Hypoxic Environment in Tumor-Stromal Cells Accelerates Pancreatic Cancer Progression via the Activation of Paracrine Hepatocyte Growth Factor/c-Met Signaling.

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Background: Pancreatic cancer is one of the representative solid tumors, in which the hypoxic microenvironment plays a crucial role in malignant progression. We previously demonstrated that tumor-stromal interaction under hypoxia enhances the invasiveness of pancreatic cancer cells through hepatocyte growth factor (HGF)/c-Met signaling. **Methods:** We investigated the immunohistochemical expression of hypoxia inducible factor-1 α (HIF-1 α), c-Met, and HGF in both cancer and stromal cells using 41 pancreatic cancer tissue specimens, and tried to identify any correlations with the clinical features and survival. **Results:** Positive staining for HIF-1 α was observed in both pancreatic cancer and the surrounding stromal cells in more than 30% of the cases, and it significantly correlated with lymph node metastasis (P < .05). A significant correlation was observed between the expression of HIF-1 α and HGF in stromal cells (P < .05). In addition, the c-Met expression in cancer cells was found to significantly correlate with the HGF expression in not only cancer but also stromal cells. The disease-free survival rates of the patients with HIF-1 α in cancer, stromal, c-Met in cancer, and an HGF expression in stromal cells was significantly worse than those without such expressions (P < .05). **Conclusions:** These data suggest that the HGF/c-Met signaling via HIF-1 α may therefore negatively affect the prognosis in patients with pancreatic cancer, and targeting tumor stroma under hypoxia might thus be potentially useful as a novel therapy for this cancer.