colorectal adenocarcinoma. In adenomas, a shift of migration indicating immunohistochemical alterations from top to the base was observed with less differentiated neoplasias. In addition Ln-5 γ2 – positive small blood vessels were detected in the invasion zone of 35% of all carcinomas, indicating a role for Ln-5 γ2 in tumour angiogenesis.
Conclusion: Our data show a distinct change of Ln-5 γ2 immunohistochemical pattern during colorectal adenoma-carcinoma-progression; adenomas with higher risk of malignant transformation or increased invasive potency can be identified by Ln-5 γ2 immunohistochemistry.

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Chemoradiation with raltitrexed and oxaliplatin in pre-operative treatment of stage II/III resectable rectal cancer: long term results of a phase II studies

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Background: The aim of the study is to evaluate the impact of a schedule of neoadjuvant chemoradiation with raltitrexed and oxaliplatin on tumor response and long-term outcome, in patients with locally advanced respectable rectal cancer.
Materials and methods: Between July 2001 and November 2002 a total of 30 patients received radiotherapy (50.4 Gy) administered to the posterior pelvis for 5 days/week for 5 weeks. Combination of raltitrexed (3 mg/m^2) and oxaliplatin (130 mg/m^2) was administered on days 1, 19, and 38. Six to 8 weeks after the end of chemoradiation patients were re-evaluated and underwent surgery. Adjuvant chemotherapy with 5-FU and leucovorin (Machover regimen) was planned to be delivered in patients with positive nodes (pN+) at pathologic examination.
Results: Tumor stage at diagnosis was: T3N0M0, 4 patients; T3N1M0, 17 patients; and T3N2M0, 9 patients. All patients underwent surgery with R0 margins. Sphincter preservation was obtained in 93% of patients. The median follow-up was 47 months (range30–61).
In all resected patients, the pathologic stages observed were: pT0N0M0, 9 patients; pT_{mic}N0M0, 6 patients; pT_{mic}N1M0, 2 patients; pT2N0M0, 3 patients; pT3N0M0, 6 patients; and pT3N1M0, 4 patients. Overall, tumor downstaging was reported in 20/30 (67%) patients and nodal downstaging in 23/30 (77%) patients with cN1–N2 stage. TRG was evaluated in all patients: TRG1, 9 patients; TRG2, 8 patients; TRG3, 8 patients; TRG4, 4 patients; TRG5, 1 patient. To date all patients are alive; no patients had relapse of local disease; the rate of metastases is 13%, with a median metastases free survival of 41 months, and a 5-years MFS of 86%. Even without any statistical significance, grouping patients according pT0–2 vs pT3, TRG1–2 vs TRG3–5 and pN0 vs pN+, we found a better results in responding patients, with a 5-years MFS of 89% in pT0–2 vs 86.5% in, 87% in TRG 1–2 vs 84% in TRG 3–5, and 86.7% in pN0 respect 83.3% in pN+.
Conclusions: Preoperative chemoradiation with novel agents showed an elevated rate of tumor response (57% had pT0 or pT_{mic}), with excellent results in terms of OS and LC, in patients with stage II/III rectal cancer. The 5-year MFS was 86%. Lower pT, TRG and pN stages seems to show a correlation with better results. A longer follow-up is required to obtain more stable results.

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Surveillance schedules and CEA workup in post operative rectal cancer patients

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Background: The follow-up of rectal cancer patients after potentially curative surgery has been shown to vary widely. The optimal schedule for such follow-up remains unknown. This study investigates the relationship between the age of the surgeon and choice of surveillance strategy.
Methods: A detailed questionnaire was sent to the 1795 members of the American Society of Colon and Rectal Surgeons (ASCRS) to measure how these specialists conduct rectal cancer follow-up. Respondents were presented with a scenario in which a rectal cancer patient (TNM stage I-III) had a potentially curative resection. They were asked how often they would use 14 separate surveillance tests during postoperative years 1–5. Repeated measures analysis of variance was used to evaluate if practice patterns were related to the year in which surgeons formal training was completed, controlling for tumor stage and year post surgery. Participants were also asked which tests they would use to further investigate a postoperative raised serum carcinoembryonic antigen (CEA), and a postoperative chest radiograph showing probable metastatic disease. Chi square analysis was used to compare practice patterns to surgeon age.
Results: Evaluable responses were received from 347 ASCRS members (19%). Repeated measures analysis of variance revealed no significant relationship between surgeon age and follow-up test ordering schedules. However, follow-up for most modalities was highly correlated with TNM stage and year post surgery, as expected. Practitioner age was a significant factor in the work-up of an elevated postoperative carcinoembryonic antigen test. An unusual relationship was observed in the work-up, with the younger and oldest surgeons ordering more complete blood counts, liver function tests, chest radiographs than the middle two age groups. Younger surgeons employed significantly more colonoscopies than all other age groups combined.
Conclusions: Our study shows that post-operative surveillance practices of surgeons caring for patients with rectal cancer do not vary with practitioner age. We propose that continued medical education (CME) has produced this standardized behavior. However, CME has been less successful in homogenizing other areas of respondent's practice, such as in the workup of a raised postoperative CEA. Therefore we conclude that practitioner age accounts for some of the variation in post-operative management of rectal cancer patients.

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Macrophages direct microscopic phenotype and clinical outcome in a colon cancer model

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Macrophages (mφ) have potent cytotoxic capacity and as such may play a role in controlling metastatic growth by killing tumor cells. By contrast, mφ, which generally constitute a major component of tumor stroma have recently also been described as promoters of tumor progression by shaping the tumor microenvironment through production of growth and angiogenic factors.
In order to gain more insight in this paradoxical role, we specifically depleted peritoneal mφ or Kupffer cells (KC; liver mφ) of Wag/Rij rats, using liposome-encapsulated dichloromethylene diphosphonate. Subsequently, CC531s syngeneic coloncarcinoma cells were injected intraperitoneally (i.p) or in the portal vein to induce i.p. or liver metastases. Rats were sacrificed on day 9 or 14, and tumors were analysed. Additionally, a survival experiment was performed.
Histopathology of tumors in both peritoneal mφ-depleted and KC-depleted animals demonstrated a high degree of differentiation (tubulo-papillary growth pattern and well-organized basement membranes) with very little stroma formation (containing no mature mφ). In contrast, tumors of control rats showed a desmoplastic stroma reaction with extensive infiltration of mφ as well as T cells, and hallmark features of malignancy, such as high vascular density, matrix remodelling and poor differentiation, indicating that presence of mφ is associated with malignant phenotype. Furthermore, mRNA profiles supported more malignant tumor growth as expression of a variety of growth factors, matrix metalloproteinases, and pro-angiogenic factors was upregulated in control tumors. Remarkably however, mφ-depleted rats bearing highly differentiated tumors displayed larger tumor load that correlated with poorer survival, supporting a crucial role in (initial) anti-tumor responses of mφ as well.
Thus, even though mφ play a role in tumor differentiation, directing the tumor into a more malignant phenotype, absence of mφ results in larger tumor load and shorter survival. This indicates that mφ exert both tumor killing and tumor promoting capacities. Anti-tumor responses, however, prevail. Selectively antagonizing mφ functions in malignant progression or enhancing tumor killing capacities might therefore represent important new targets for cancer therapy.

686 PUBLICATION

Expression of matrix metalloproteinase-7 and matrix metalloproteinase-9 and its prognostic significance in rectal cancer

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Background: The matrix metalloproteinases (MMPs) are a family of proteolytic enzymes involved in tumor invasion; several individual members