of which have been implicated in tumor prognosis. The aim of this study was to evaluate the prognostic significance of MMP-7 and MMP-9 in rectal cancer.
Methods: Eighty-seven patients with stage II or III rectal carcinoma who underwent potentially curative resection followed by postoperative adjuvant chemoradiation, and 5-fluorouracil based chemotherapy were investigated immunohistochemically using the monoclonal antibody MMP-7 and MMP-9. Clinical information, including tumor grade, carcinoembryonic antigen (CEA), disease-free survival (DFS), and overall survival (OS) was evaluated and compared with MMP-7 and MMP-9 expression.
Results: The median follow-up duration was 53.2 months, and mean patient age was 55±11 years (range 32–75). The expression of MMP-7 correlated significantly with the presence of nodal metastasis ($P = 0.029$). MMP-9 expression was significantly correlated with the depth of tumor invasion ($P = 0.019$). No relationships were found between the MMP-7 and MMP-9 expression and age, sex, tumor size, tumor grade, or CEA level. Univariate analysis showed that MMP-7 expression was associated with poor 5-yr OS (12.8 months vs. 65.3 months, $P = 0.0405$). Multivariate analysis confirmed that MMP-7 was independently associated with adverse outcome (Relative risk: 1.415, $P = 0.027$). However, MMP-9 expression was not related to clinical outcomes.
Conclusion: MMP-7 expression was associated with lymph node metastasis and poor 5-year OS in rectal cancer patients.

687 PUBLICATION

Abdominoperineal resection or anterior resection for rectal cancer: study of patients' preferences before and after treatment

A. Zolciak[1], K. Bujko[1], L. Kepka[1], J. Oledzki[2], A. Rutkowski[2], M. Nowacki[2]. [1]*Cancer Center of Oncology, Department of Radiotherapy, Warsaw, Poland;* [2]*Cancer Center of Oncology, Department of Colorectal Cancer, Warsaw, Poland*

Purpose: The data in the literature do not allow for the conclusion that the oncological outcomes and the quality of life after anterior resection (AR) are superior to that after abdominoperineal resection (APR). Therefore, patients' preference remains a main reason for performing AR for low rectal cancer. The aim of the study is to evaluate these preferences.
Methods: Consecutive patients with rectal cancer (60 prior to surgery, 65 with permanent colostomy and 124 after AR) who visited our out-patient clinic answered the questionnaire on preferences for type of surgery.
Results: Preferences for APR, for AR or for leaving decision to a physician were respectively following: prior to surgery group – 5, 30, 65 per cent; permanent colostomy group – 46, 22, 32 per cent and AR group – 4, 68.5, 27.5 per cent. Among patients after surgery who had definite preferences, those after AR more frequently preferred the undergone type of surgery than those with permanent colostomy; 94 vs. 68 per cent, respectively, $P < 0.001$.
Conclusions: As the small percentage of patients prior to surgery prefers the APR, a shared decision-making process is of value for those with a low rectal cancer. The results suggest that for patients who underwent surgery, sequels after AR are generally perceived as less severe than those after APR. Nevertheless, approximately half of the patients after APR prefers undergone type of surgery, which suggests that perception of a colostomy as a bearable status is higher than it is commonly believed.

688 PUBLICATION

Does the surgical scalpel act the role of the second fiddle in the battle against lower two-third rectal cancers? A 5-year follow up study

M. Gábor[1], H. Urbancsek[2], T.I. Szendrő[1], M. Török[3], Z. Szabad[1], Á. Horváth[2]. [1]*Kenézy Teaching County Hospital, Gen. Surgery, Debrecen, Hungary;* [2]*University of Debrecen, Department of Radiation Oncology, Debrecen, Hungary;* [3]*Kenézy Teaching County Hospital, Dept. of Pathology, Debrecen, Hungary*

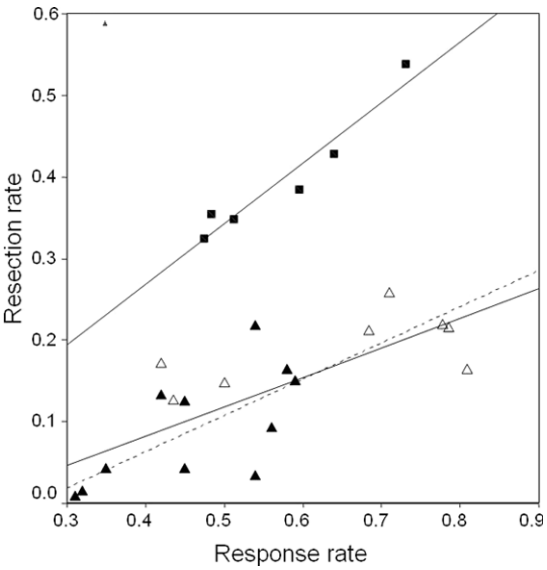
Background: Gold standard therapy of lower two-third rectal neoplasms is a hotly debated point of the onco-radio-surgical complex treatment, and it is source of boiling discussions.
Aims: The authors' aim was to evaluate a 5-y follow-up study regarding to T1–4, N0–2, M0 rectal cancers.
Patients and method: Four groups were set up, in each group was 50 patients with lower two-third T1–4 N0–2 stage (there were proved these stages by CT, MRI or rectal USG) rectal cancer. In the first group the patients had been given 50.4 Gy so-called long term three-field irradiation and three or at least two cycles of 5FU base chemotherapy. In the second one the patients had been given 50.4 Gy irradiation, in the third one they had been given a short term (4×4 or 4×5 Gy) irradiation before surgical intervention. The fourth one was the control group (following surgical intervention an adjuvant standard chemo-iradiation). The down staging was strictly examined after neoadjuvant treatments by CT, MRI or rectal USG) There has been examined the overall survival (OS) time to relaps (TR) and disease free survival (DFS). The results were analysed by statistically.
Results: Histologically proved total remissions were detected only in the first and second group (4 and 7 patients, respectively). Proportion of clinical response in the three groups were 28%, 18% and 0%, respectively. Proportion of local failure was 12%, 14% and 20%, respectively. The difference between the groups were significant. Histologically proved total remissions were detected only in the long-term irradiated groups, though there is a significant difference depending on whether the patients had been given chemotherapy or not, alongside of the irradiation. There have not been detected local failurs at all in the cases of clinical and histological total remissions after surgical interventions. Total remission has not occurred in stage of T4. Only three patients out of 200 were grouped in stage T1.
Discussion: The 5-y-survival in cases of total preoperative remission was nearly 100%. It is startingly few the number of patients with early (T1) disease, and it seems that the proportion of early diagnosis won't change in the future without consistent and well-organised screening systems. In stage of T2 and T3 the neoadjuvant long term irradiation with or without chemotherapy can bring significantly better result than short term irradiation or the adjuvant treatment. In stage of T4 the chance for a successfully radical operation was significantly better after combined long term irradiation with chemotherapy than in the other three groups.
Conclusion: The authors recommend on the first place the method of long term three-field neoadjuvant irradiation combined with chemotherapy for T2–4 rectal neoplasms. The authors have proved the advantage of neodjuvant treatment for rectal cancer instead of primarily used surgical intervention. It is possible that the surgical scalpel is inevitable part of the treatment these days but its main role must be shared with other pretenders.

690 PUBLICATION

Correlation of the rate of liver resection to the rate of tumor response in patients with metastatic colorectal cancer

G. Folprecht[1], A. Grothey[2], S. Alberts[2], H.-R. Raab[3], C.-H. Köhne[3]. [1]*University Hospital Dresden, Medical Dept. I, Dresden, Germany;* [2]*Mayo Clinic, Rochester, MN, USA;* [3]*Klinikum Oldenburg, Oldenburg, Germany*

Introduction: Long-term survival is reported in patients with liver metastases of colorectal cancer. Recently, an increased number of reports on liver resection following neoadjuvant chemotherapy in patients with initially unresectable liver metastases has been published.
Methods: We analyzed all published or presented trials and retrospective studies that report the rate of objective response and the rate of resection of initially unresectable metastases to correlate of objective response and the rate of resection of metastases.



Results: In studies that enrolled patients with metastases confined to the liver, 24 to 54% of patients were resected following chemotherapy, compared to 1 to 26% of patients in trials that included non-selected patients with metastatic colorectal cancer. A strong correlation was found between response rates and the resection rate in studies with patients with

isolated liver metastases (r = 0.96, p = 0.002). Likewise in studies with non-selected patients, the resection rate of metastases also was associated with the objective response rate (r = 0.74, p < 0.001).
Conclusion: Patient selection and efficacy of pre-operative chemotherapy are both strong predictors for resectability of liver metastases. Resectability is a novel endpoint focusing on the curative potential of treatment compared with classical endpoints of response or progression free survival that are important if palliation is the aim. Therefore, patients with potentially resectable liver metastases should be investigated in special trials and interdisciplinary teams.

691 PUBLICATION

Tissue inhibitor of metalloproteinases 1 (TIMP-1) as an immunohistochemical marker for colorectal cancer

I. Sorensen[1,2], H. Winther[2], N. Foged[2], C. Fenger[3], N. Brünner[1].
[1]Royal Veterinary and Agricultural University, Vetereinary Pathobiology, Frederiksberg, Denmark; [2]DakoCytomation, Glostrup, Denmark; [3]Odense University hospital, Pathology, Odense, Denmark

Background: TIMP-1, which is an endogenous inhibitor of the proteolytic activity of matrix metalloproteases (MMP) is present in elevated concentrations in plasma from colorectal cancer patients, and is a promising circulating marker for use in the early detection of colorectal cancer. In addition, measurement of plasma TIMP-1 has been suggested as a tool for prognostic separation of patients with early stage colorectal cancer. Recent studies based on *in situ* hybridisation and immunohistochemistry (IHC) have demonstrated that TIMP-1 mRNA and protein is expressed infibroblast-like cells in the invasive front of colorectal adenocarcinomas, while seen only sporadically in normal mucosa.
Aim: The aim of the present study was to investigate if detection of TIMP-1 by IHC can be used for the early diagnosis of colorectal cancer.
Materials and methods: The presence of TIMP-1 was studied in paraffin-embedded archival colorectal adenoma (n = 77) and adenocarcinoma (n = 46) samples obtained from The University Hospital of Odense, Denmark. An indirect IHC technique was employed by using the monoclonal mouse antibody from clone VT-7 and the ChemMate™ EnVision™ Detection Kit from DakoCytomation. Pre-treatment of the tissue was performed using a heat induced antigen retrieval protocol including DakoCytomation's Target Retrieval Solution (S1700). Negative control antibodies matched the isotype and concentration of the VT-7 antibody.
Results: A distinct TIMP-1 immunoreactivity was observed in scattered fibroblast-like cells localized to the invasive front of the majority of the colorectal carcinomas, whereas TIMP-1 immunoreactivity in tumor cells was only seen in a few cases. Furthermore, the IHC showed a pale immunoreactivity of some of the epithelial cells in the adenomas and also a few single epithelial cells in the normal mucosa. The negative control antibodies displayed no staining.
Conclusion: This study confirms the expression of TIMP-1 protein in the fibroblast-like cells in association with invading colon cancer cells. It also shows that while most adenocarcinomas show TIMP-1 immunoreactivity in the stromal cells of the tumors, no stromal TIMP-1 immunoreactivity was observed in the adenomas. These data suggest that stromal TIMP-1 immunoreactivity may be used as a mean to distinguish between adenocarcinomas and adenomas of the colon.

692 PUBLICATION

Preoperative chemoradiation in rectal cancer: retrospective comparison between capecitabine and continuous infusion of 5-Fluorouracil

R. Yerushalmi[1], E. Idelevitch[2], I. Dror[3], S.M. Stemmer[1], A. Figer[4], A. Sulkes[1], D. Loven[5], B. Brenner[1], A. Shani[2], E. Fenig[1]. *[1]Rabin Medical Center, Beilinson Campus, Institute of Oncology, Petach Tiqva, Isreael; [2]Kaplan Medical Center, Institute of Oncology, Rehovot, Isreael; [3]Sapir Medical Center, Instituite of Oncology, Kfar Saba, Isreael; [4]Sourasky Medical Center, Instituite of Oncology, Tel-Aviv, Isreael; [5]Ha'Emek Medical Center, Institute of Oncology, Afula, Isreael*

Background: We compared the efficacy and toxicity of oral capecitabine and continuous infusion of 5-fluorouracil (5-FU) in the preoperative chemoradiation treatment of patients with rectal cancer.
Patients and Methods: The files of 89 patients with rectal cancer, 43 treated preoperatively with oral capecitabine and 46 with intravenous 5-FU, were reviewed, and the outcome of the groups was compared.
Results: There was no statistically significant difference in the complete pathological response rate between the capecitabine and the 5-FU group (30% vs. 17%, p = 0.15). The downstaging rate was higher in the capecitabine group (77% vs. 50%, p = 0.009). Toxicity was mild in both groups. The rate of grade 3 gastrointestinal toxicity was similar in the two groups (diarrhea 2% vs. 4%, proctitis 5% vs. 7%), except for one patient in the 5-FU group (2%) who developed a rectovaginal fistula. In the capecitabine group, one patient (2%) had grade 3 hand–foot syndrome, and another had an acute myocardial infarction. In the 5-FU group, 2 patients (4%) had grade 3 hematological toxicity, and 3 (6%) had complications from Port-a-Cath insertion.
Conclusion: Preoperative chemoradiation with oral capecitabine appears to be safe and well tolerated, and at least as good as continuous 5-FU for the neoadjuvant treatment of rectal cancer.

693 PUBLICATION

Preoperative neoadjuvant radiochemotherapy for rectal adenocarcinoma

J. Dvorak[1], R. Voboril[2], P. Hladik[2], P. Vesely[1], B. Melichar[1], J. Petera[1], Z. Zoul[1], M. Vosmik[1], P. Jandik[2], J. Mergancova[2]. *[1]Charles University Hospital, Oncology and Radiotherapy, Hradec Kralove, Czech Republic; [2]Charles University Hospital, Surgery, Hradec Kralove, Czech Republic*

Purpose: To evaluate retrospectively the efficacy and toxicities of preoperative neoadjuvant radiochemotherapy for locally advanced rectal adenocarcinoma.
Patients and Methods: Between April 2000 and March 2004, 81 patients (pts), 62 males and 19 females, mean age 64 (41–78) years, with locally advanced undisseminated rectal cancer (cT3–4, and/or N+, M0), were treated. All pts had histology of adenocarcinoma: 8 pts grade 1, 56 pts grade 2 and 17 grade 3. Radiochemotherapy consisted of external beam radiotherapy 45–50.4 Gy in 25–28 fractions, 1.8 Gy daily, with concomittant chemotherapy: 5-fluorouracil 200 mg/m^2/day in continuous infusion. Surgery was performed 5–6 weeks after the end of radiochemotherapy.
Results: The median of pre treatment CEA level was 3.84 (0.95–107.1) mg/l. The median of pre treatment hemoglobin level was 137 (63–196) g/l, leucocytes 7.6 (4.1–13.06) 109/l and thrombocytes 248 (99–455) 109/l. The median of nadir during radiochemotherapy was as follows: hemoglobin level 128 (93–152) g/l, leucocytes 4.7 (1.6–17.11) 109/l and thrombocytes 191 (38–281) 109/l. Grade 3 leucopenia occurred in 2 pts, grade 3 thrombocytopenia in 1 pt, diarrhea grade 3 in 4 pts. One pt didn't complete planned regimen of radiochemotherapy because of leucopenia. After neoadjuvant preoperative radiochemotherapy was achieved radical resection with microscopically negative margins (R0) in 72 (89%) pts [43 (54%) pts sphincter-preserving resection and 29 (35%) pts abdomino-perineal resection], resection with microscopic residual tumor (R1) in 2 pts and resection with macroscopic residual tumor (R2) in 7 (9%) pts. Pathologic TNM stage after neodjuvant radiochemotherapy was as follows: 7 (9%) pathologic complete response, 20 (24%) pts stage I, 36 (45%) pts stage II, 12 (15%) pts stage III and 6 (7%) pts stage IV. Downstaging after neoadjuvant radiochemotherapy was achieved in 42 (52%) pts. At the date of evaluation (April 30th, 2005) 58 pts were alive. One-year survival was 96.3% (95% CI: 92.1%-100%). Two-years survival was 81.8% (95% CI: 72.6%-90.8%). Three-years survival was 63.5% (95% CI: 50.2%-76.9%). Twenty-two pts (27%) have recurrence: 11 (13.5%) local recurrence and 11 (13.5%) distant metastases (7 pts liver metastases, 3 pts pulmonary metastases and 1 pt brain metastases).
Conclusions: This study demonstrates the efficacy and toxicities of preoperative neoadjuvant radiochemotherapy for locally advanced rectal adenocarcinoma.

694 PUBLICATION

5-fluorouracil and l-leucovorin by night infusion chronotherapy and pelvic radiotherapy combined with regional hyperthermia in patient with advanced or recurrent rectal carcinoma

H. Sakurai[1], T. Asao[2], M. Shioya[1], K. Harashima[1], T. Nonaka[1], Y. Suzuki[1], T. Nakano[1], S. Yamaguchi[2], S. Tsutsumi[2], H. Kuwano[2].
[1]Gunma University Graduate School of Medicine, Radiation Oncology, Maebashi, Gunma, Japan; [2]Gunma University Graduate School of Medicine, General Surgical Science, Maebashi, Gunma, Japan

Background: To investigate an effect of 5-fluorouracil and l-leucovorin by night infusion chronotherapy and pelvic radiotherapy combined with regional hyperthermia in patient with advanced or recurrent rectal carcinoma in a preoperative setting.
Material and Methods: Between January 2003 and March 2005, 33 patients including 4 locally recurrent cases were entered onto this study. The patients were staged as follows according to the UICC classification: 4 in T2, 26 in T3 and 3 in T4. The external irradiation was delivered with a three-field technique with daily 2 Gy per fraction at a total dose of 40 Gy (initial 11 cases) to 50 Gy (later 22 cases) to the tumor site and surrounding lymph nodes. Two cycles of chemotherapy were given on weeks 2 and 4, with 5-day night infusion (12 hr) of 5-fluorouracil (5-FU)