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

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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

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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

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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

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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)

250 mg/m^2/day+ l-leucovorin (l-LV) 25 mg/body/day. Weekly hyperthermia was performed for 60 min immediately after irradiation for 3 to 5 sessions with radiofrequency capacitive heating devices. Surgery was planned 6 to 8 weeks later. Treatment response was evaluated with high resolution MRI. After the operation, histological examination was also performed.
Results: All patients completed treatment without treatment modification. For hyperthermia, overall average value of maximum temperature in rectal cavity was 40.1ºC. Grade 2, 3 and 4 acute diarrhea (NCI-CTC version 2) occurred in 6.1%, 3.0% and 0%, respectively. Tumor down staging using high resolution MRI occurred in 16 (48.5%) cases. There was 79.2% (19/24) agreement between preoperative MRI and pathology assessment of T stage. After the preoperative treatments, clinical complete response (tumor was not detected by MRI, colon fiberscope, and residual cancer tissue also remained unproved histologically) were seen 30.3% (10/33). Surgery was performed in 25 of 33 patients. The remainder has not received surgery (development of metastasis in 2, refused surgery in 3, within 6 weeks from completion of preoperative therapy in 3). Sphincter preserved surgery was performed in 17 patients (68.0%). No macroscopic tumor with only pathological microscopic disease was observed in 24.0% (6/25), and pathological complete response was observed in 12.0% (3/25).
Conclusions: The use of 5-fluorouracil and l-leucovorin by night infusion chronotherapy and pelvic radiotherapy combined with regional hyperthermia increases tumor response with less adverse effects and may contribute to increased sphincter preservation in patients with low rectal cancer.

695 PUBLICATION

CT investigations in contemporary decision making of CD 117 revised gastrointestinal stromal tumours (GISTs)

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Background: The management of GISTs has evolved very rapidly since the introduction of tyrosinekinase inhibitors. Many GISTs were not recognized in the past, but recently developed immunohistochemical markers have facilitated their diagnosis. We reevaluated the clinico-pathological features of previously resected mesenchymal tumours of the gastrointestinal tract. The aim of this study was to determine the accuracy of previous diagnoses and to investigate whether subsequent CT-investigations would reveal new (treatable) lesions in case of GIST.
Patients and methods: Patients with mesenchymal tumours of the gastrointestinal tract operated on between 1987 and 2005 were identified using medical and pathology files (PALGA). These tumours were pathologically reviewed using immunohistochemical staining for CD 117, CD 34, MIB 1, S100 and actine, a procedure which has been performed as a standard since 2002. Patients alive and identified as GISTs underwent pulmonary and abdominal CT-scans in order to identify individuals suitable for further (imatinib) treatment.
Results: 41 Tumours had been identified as possible GISTs in this period. 32 Mesenchymal tumours of patients still alive were reanalyzed. Of these, 13 tumours had correctly been identified as GISTs. Pathological revision of the other 19, previously diagnosed as undefined gastrointestinal mesenchymal tumours, revealed GIST in another 8 cases. Therefore 21 of 32 (66 %) gastrointestinal mesenchymal tumours were shown to be GISTs. At surgery 19 GIST-patients underwent a R0 resection. In one patient a R2 resection was performed and in one patient the tumour appeared to be irresectable at time of operation. The latter two patients started imatinib immediately postoperatively. In 7 of the remaining 19 patients a CT-scan was not performed because of old age (>80 years). Until now in three of the remaining 12 patients CT-scanning showed loco-regional and metastatic disease, where after imatinib was started.
Conclusions: The true incidence of GISTs has been underestimated. There is a merit in reviewing the clinical diagnoses of all mesenchymal tumours of the gastrointestinal tract using modern immunohistochemical techniques. In case of GIST, follow-up schemes using pulmonary and abdominal CT-scanning can detect loco-regional or metastatic disease which may respond to surgical resection and/or imatinib treatment.

696 PUBLICATION

A pragmatic basis for follow up of patients after hepatectomy (HPX) for colorectal liver metastases (CLM)

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Introduction: HPX is the only treatment for CLM that offers potential cure. However >60% of cases will recur after HPX for CLM, and patients increasingly are undergoing repeat-HPX with further curative intent. However there is no consensus regarding the timing of follow-up CT scans following HPX for CLM. These scans are expensive, involve considerable radiation exposure, add psychological morbidity and are only of use if they detect potentially treatable recurrent disease. This study evaluates timing of detection of liver only recurrence (LOR) post-HPX and its relationship to further possible liver surgery on which to base a pragmatic follow-up protocol.
Methods: Prospective single centre 5-yr follow-up of 184 patients post-HPX for CLM. Data stratified and presented as number of patients for timing and site of LOR, extra-hepatic recurrence (HER), repeat-HPX with curative intent.
Results: 108/184 (59%) developed recurrent disease during the first 5 years after HPX, and 14 were amenable to repeat-HPX.

Time of detection (months)	LOR	EHR	Repeat-HPX
3	1	4	0
4–6	21	10	1
7–9	13	5	3
10–12	10	11	3
13–18	6	3	2
19–24	5	2	2
25–60	8	9	3

Conclusions: Very few cases recurring <6 months post-HPX were amenable to repeat-HPX. The peak incidence of LOR amenable to repeat-HPX occurs between 6–24 months post-HPX. Therefore a reasonable follow up protocol for post-HPX CT scans would be at 6, 12, 24, 36, 48 and 60 months post-HPX.

697 PUBLICATION

Preoperative criteria of incomplete resectability of peritoneal carcinomatosis from non-appendiceal colorectal carcinoma

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Objective: to analyse the causes of non resectability of peritoneal carcinomatosis (PC) of non-appendiceal colorectal carcinomas, discovered only at the time of the laparotomy.
Background: The combination of a maximal cytoreductive surgery (resecting tumor deposits >2 mm of diameter) with intraperitoneal chemo-hyperthermia results in curing a significant number of patients. Complete resectability of PC is the determining factor of this time-consuming and resource-consuming therapy. Unhappily, we have not been able, so far, to safely predict this resectability before laparotomy.
Methods: We prospectively checked the selected patients with colorectal PC who underwent a laparotomy in order to receive this new treatment, but who finally presented a non completely resectable PC. Their preoperative parameters were retrospectively studied and compared to those of the same number of similar mixed patients who successfully underwent this treatment.
Results: 29 patients presented a non completely resectable PC at laparotomy. They were compared with 29 other mixed patients who underwent a complete resection of the PC. The factors allowing to predict this non resectability were, in a decreasing order: presence or persistence of an ascitis just before the laparotomy ($p = 0.0008$), progression of the PC while on neo-adjuvant chemotherapy ($p = 0.01$), abnormal CT-imaging ($p = 0.03$), and subocclusive syndroma ($p = 0.05$). These parameters were partially interrelated.
Conclusion: The persistence of an ascitis, and any progression of the disease while on chemotherapy are important predictive factors of incomplete resectability of non-appendiceal colorectal PC.