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Impact of multimodality approach to patients with colorectal cancer. The experience of a hospital registry of tumors

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Introduction: Colorectal cancer (CRC) is the third tumor in relevance in our area. The high incidence of this tumor makes mandatory an accurate analysis of the impact of multidmodality treatment in the survival of affected patients (pts).

Objective: To determine the relative survival of pts afected by CRC diagnosed and/or treated in our sanitary area analysed by age, sex and tumoral stage since 1993, date of implementation of a systematic, multimodality treatment of CRC.

Patients and methods: From 1993 to 1997, 1528 pts affected of CRC were registred in our Hospital Registry of Tumors (HRT). We crossed our data with data from Regional Registry of mortality in order to know the vital state and reason of death. The observed survival rate was determined by Kaplan-Meier method, the expected survival rate by Cox model using the Regional population death tables. Relative survival rate was calculated as the quocient between observed and expected survival rate. We compared our results with other results reported from USA, Surveillance Epidemiology and End Results Registry (SEER) and Europe, EUROCARE.

Results: Relative survival in women with CRC was 0.59 (0.54-0.66) and in men 0.57 (0.52-0.62). In Europe, five years survival was: women 0.41-0.56 and men 0.40-0.56. Survival analysis by stage in our HRT was for women Stage (E) I 0.96 (0.83-1), EII 0.82 (0.71-0.81), EIII 0.60 (0.51-0.71), EIV 0.09 (0.06.0.23), unknown E 0.34 (0.20-0.57). And for men EI 0.86 (0.73-1), EII 0.74 (0.65-0.85), EIII 0.5 (0.40-0.62), EIV 0.17 (0.10-0.19), unknown E 0.36 (0.25-0.53).The existence of a "hospital byass" can be observed when focusing differences in distribution by stages between HRT and SEER (HRT: I 11.4%, II 28.9%, III 33.2%, IV 15.6%, Unknown 10.8%; SEER: I 17.1%, II 28.1%, III 21.1%, IV 17.1%, unknown 16.6%). Five years relative survival in HRT/SEER were: I 0.90/0.90, II-III 0.66/0.65, IV 0.14/0.08, unknown 0.35/0.34.

Comclusions: These results show that survival in CRC in our HRT is better than the one observed in Europe and similar to SEER. Although we cannot apply these results to a general population we can conclude that a multimodality approach to these pts with a good oncologic surgery with high index of salvage resections and a correct coordination with chemo-radiotherapy treatments leads to an improvement in survival. Using hospital survival analysis we will be able to evaluate further therapeutic approaches in oncology.

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Preoperative (chemo)radiotherapy for rectal cancer: Influence of treatment schedule on locoregional control

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Purpose: To assess the influence of two different preoperative schedules on down staging and local control.

Material & Methods: 118 patients with adenocarcinoma of the rectum were referred for preoperative radiation between 1995 and 2000. Local tumour extension was assessed by clinical examination, echoendoscopy and CT scan of the pelvis. There were 7 Stage I tumours, 39 stage II and 72 stage III. In 72 patients the tumour was located ≤6 cm from the anal margin. Two different preoperative schedules were used: 54 patients were treated with 10 times 3 Gy followed by surgery 38 days (14–58 days) later, the other group of 64 patients were treated with 25 times 1.8 Gy combined with 5-FU, LV during the first and last 5 days of irradiation. The interval between the last day of irradiation and surgery was 41 days (14–111 days) in these patients. In 55% of the cases postoperative adjuvant chemotherapy was given.

Results: Local control at 1, 2 and 3 years was 100%, 96%, 90% respectively, disease free survival was 97% at 1 year, 87% at 2 years and 77% at 3 years. There was no statistically significant difference in T-stage ($X^2 = 4.98$, $p > 0.05$) or distance of the tumour from the anal margin ($X^2 = 0.77$, $p > 0.05$) between the two patient groups; the number of patients with clinically positive nodes was higher in the group treated with preoperative combined modality treatment ($X^2 = 9.44$, $p \leq 0.025$). The anal sphincter was preserved in 82 patients (69%); in 60 patients a TME with construction of a colo-anal J-pouch was performed. Sixty three percent of these patients had a temporary protective ileostoma. Down staging, defined as a reduction in the pathological stage compared to the clinical stage, was obtained in 60 patients (51%), 26 of these patients were treated with the short schedule. In 15 patients (13%) there was no residual tumour left in the resection specimen. Only 4 of these patients were treated with 30 Gy in 10 fractions. Seven patients developed a local recurrence, 3 of these were irradiated to a total dose of 30 Gy. Distant me-tastasis were detected in 18 patients, 10 of them were treated with the short schedule.

Conclusion: There was no significant difference in down staging or local control between the short and the long irradiation schedule. The anal sphincter could be preserved in 73% of the patients. The upfront use of chemotherapy had no statistical significant influence on sphincter preservation or down staging, although more complete regressions were obtained in the patients treated with the combined modality.

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BAX protein expression (BAX-E) correlates with local invasiveness in primary colon cancer (CC)

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Purpose: The existing multimodal treatment options for CC require better prognostic markers to adapt treatment strategies to the individual patients' tumour biology. An imbalance between apoptosis and proliferation is believed to influence the course of malignancies. Recent work has shown that pro-apoptotic Bax-E. in liver metastasis is of prognostic significance in stage IV CC. We sought to test the prognostic role of Bax-E. in primary CC.

Methods: Archival tumour specimens of 371 pats. with Dukes A, B or C CC were retrieved. All pats. underwent R0-surgery in one singular institution and did not receive adjuvant chemotherapy. Follow up was performed in accordance to a standardized protocol (median follow-up 31.6 months). Bax-E. was determined by semi-quantitative immunohistochemical assessment (AB N20, Santa Cruz, USA).

Results: Bax-E. was detected in 353 of the samples (95.1%). Overall staining of 100% of the tumor cells was detected in 141 samples (38.0%). 18 (4,9%) showed no staining at all. The mean percentage of Bax expressing cells was 91.5%. Evaluation of the percentage of positive cells, the staining intensity and the Bax index involving both intensity and percentage of Bax positive cells failed to show a significant influence on overall survival (OS), Nor did disease free survival (DFS) correlate to Bax staining properties. OS was rather influenced by the UICC stage,disease relapse and age. Interestingly Bax staining intensity and the Bax index correlated to the invasion stages of the tumor (p=0.015 and 0.013 respectively) and the grade of differentiation (G category p=0.001).

Conclusion: Neither the percentage of bax positive tumour cells nor the intensity of bax expression proved to have a prognostic significance in regard to OS or DFS. However, a decrease of Bax-E. showed a significant correlation with higher depth of tumour invasion (T category) and the differentiation grade. It is concluded, that bax contributes to the local aggressiveness and invasion but that overall prognosis in CC, which most often is determined by the development of distant metastasis, is most certainly influenced by other factors.

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Role of the DNA mismatch repair system in the responsiveness of metastatic colorectal cancers to chemotherapy with CPT-11 (Irinotecan)

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The aim of our study was to assess the potential relationship between the microsatellite instability (MSI), a feature of tumors with DNA mismatch repair defect, and the response to CPT-11 treatment. Fifty patients with metastatic