show a putative involvement of the kinase Ret (known to phosphorylate the Y654 site of beta-catenin) upstream in the pathway activated by the mechanical deformation. Treatment during compression with Sunitinib, a specific inhibitor of Ret, impairs Ret pY1062 phosphorylation, in the same way as beta-catenin nuclear translocation and Twist and c-Myc gene expression. We propose that strains associated to intestinal transit or tumour growth triggers the activation of the primary oncogene program in genetically predisposed pretumoral APC+/− mice colon tissues *ex vivo*. Nowadays our goal is to check the effect of different specific Ret kinase inhibitors on this mechano-sensitive oncogenic pathway and test its impact on tumour progression *in vivo*.

6029 POSTER

Osteopontin Enhanced Hepatic Metastasis of Colorectal Cancer Cells

L. Ding[1], H.G. Hu[1], S. Zheng[2]. [1]*Second Affiliated Hospital Zhejiang University College of Medicine, Medical Oncology, Hangzhou, China;* [2]*Second Affiliated Hospital Zhejiang University College of Medicine, Cancer Institute, Hangzhou, China*

Background: Liver metastasis is a major cause of mortality from colorectal cancer (CRC). However, the underlying mechanisms are largely unknown. Osteopontin (OPN) is a secreted phosphorylated glycoprotein that is involved in tumour migration and metastasis. But the whole story of OPN relating to cancer has been far from clear to date.
Material and Methods: OPN mRNA was examined in tissues from CRC, adjacent normal mucosa and liver metastatic lesions using quantitative real-time PCR analysis. The protein expression of OPN and its receptors (integrin αv and CD44 v6) was detected with immunohistochemical (*IHC*) method. The role of OPN in liver metastasis was studied in established colon cancer Colo 205 and SW480 cells lines transfected with sense- or antisense-OPN eukaryotic expression plasmids. Florescence redistribution after photobleaching (FRAP) was used to study gap functional intercellular communication (GJIC) among OPN-transfected cells.
Results: It was found that OPN was highly expressed in metastatic hepatic lesion of CRC compared to primary CRC tissue and adjacent normal mucosa. OPN expression was also detected in normal hepatocytes surrounding CRC metastatic lesion. Two known receptors of OPN, integrin αv and CD44v6 proteins, were strongly expressed in hepatocytes of normal liver. Colon cancer cells with forced OPN expression exhibited increased heterotypic adhesion with endoepithelial cells and weakened intercellular communication.
Conclusions: OPN is playing a significant role in CRC metastasis to liver through interaction with its receptors in hepatocytes, decreased homotypic adhesion and enhanced heterotypic adhesion.

6030 POSTER

The Number of High Risk Factors is Related to Outcome in Stage II Colonic Cancer Patients

B. Koebrugge[1], D.J. Lips[1], F.J. Vogelaar[1], J.F. Pruijt[2], J.C. van der Linden[3], M.F. Ernst[1], K. Bosscha[1]. [1]*Jeroen Bosch Hospital, Surgery, 'S Hertogenbosch, The Netherlands;* [2]*Jeroen Bosch Hospital, Internal Medicine/Oncology, 'S Hertogenbosch, The Netherlands;* [3]*Jeroen Bosch Hospital, Pathology, 'S Hertogenbosch, The Netherlands*

Background: A subgroup of stage II colonic cancer patients are considered to be at high risk for recurrent/metastatic disease based on 1) tumour obstruction/perforation 2) <10 lymph nodes 3) T4 lesions and 4) lymphangio-invasion. Their prognosis is regarded as comparable to stage III colonic cancer and it is therefore strongly advised to treat them with adjuvant chemotherapy. The purpose of this study was *i)* to determine the magnitude of prognostic significance of the conventional high risk factors and *ii)* to determine whether the number of high risk factors influences outcome.
Materials and Methods. We retrospectively analyzed 212 stage II colonic cancer patients undergoing surgery between January 2002 and December 2008. No adjuvant chemotherapy was given.
Results. 154/212(73%) patients were considered to be high risk patients based on conventional high risk factors. 58 patients did not meet any high risk factor, 125 patients met 1 high risk factor and 29 patients met ⩾2 high risk factors. Median follow up was 40 months.
Multivariate analysis identified four independent risk factors for recurrent/metastatic disease: age, obstruction, perforation and lymphangio-invasion.
The three-year-DFS-rates for the low-risk group, the high-risk group with 1 high-risk-factor and the high-risk group with ⩾2 high-risk-criteria are 90.4%, 87.6% and 75.9% respectively.
Patients meeting ⩾2 conventional high risk criteria had a significantly worse three-year-disease free survival ($p < 0.002$).
Conclusions. Four independent high risk factors were identified. The number of high risk factors does influence outcome. Therefore, patients with ⩾2 high risk factors should receive adjuvant chemotherapy without any hesitation.

6031 POSTER

Combined Neoadjuvant Chemoradiotherapy With Radiosensitization Shows Good Response and Low Toxicity Rate in Locally Advanced Rectal Cancer Treatment

S.S. Gordeyev[1], V.V. Glebovskaya[2], E.N. Halavka[3], S.T. Mazurov[4]. [1]*Blokhin Cancer Research Center, Proctology, Moscow, Russian Federation;* [2]*Blokhin Cancer Research Center, Radiational Oncology, Moscow, Russian Federation;* [3]*Blokhin Cancer Research Center, Radiology, Moscow, Russian Federation;* [4]*Blokhin Cancer Research Center, Endoscopy, Moscow, Russian Federation*

Background: Resectability is a major issue for locally advanced fixed or tethered rectal cancer. The search for new ways to improve neoadjuvant treatment effect without increasing toxicity is an important research direction. The aim of this trial was to evaluate treatment response and toxicity rate after chemoradiotherapy with local hyperthermia and metronidazole as radiosensitizers.
Methods: From July 2006 to February 2011, 74 previously untreated patients were enrolled. The external dose of radiotherapy was 40 Gy given in 10 fractions 3 times per week. Oral capecitabine 650 mg/m^2 bid was given on days 1−22 and intravenous oxaliplatin 50 mg/m^2 was administered on days 3, 10, 17. Local high-frequency hyperthermia 41–45^{0}C during 60 minutes was performed on days 8, 12, 15, 17. Metronidazole 10 g/m^2 was administered per rectum on days 12 and 17. Surgery was carried out within 6−8 weeks after neoadjuvant treatment. Tumour regression was measured according to Dworak scale. Toxicity was evaluated by NCI-CTC v 3.0 criteria.
Results: Grade I-II toxic events were observed in 34 (45.9%) patients. Grade III events included diarrhea − 14.9% (n = 11), vomiting − 2.7% (n = 2) and proctitis − 2.7% (n = 2). No grade IV events were observed. Five patients (6.7%) remained inoperable. All 69 (93.3%) patients with resected tumour had R0 resection. Eight patients had grade IV regression (10.8%), 29 patients had grade III regression (39.2%).
Conclusions: Investigated treatment scheme with radiosensitization demonstrates encouraging treatment response rate, while toxicity remains comparable to standard regimens.

6032 POSTER

Colonic Tumour Localization, Clinicopathological Patterns and Incidence of Colorectal Carcinoma in Mexican Population

E. Ruiz-Garcia[1], H. Astudillo-de la Vega[2], J.L. Aguilar-Ponce[3], J. Martinez-Cedillo[3], A. Meneses-Garcia[4], G. Calderillo-Ruiz[1]. [1]*INCan, Gastro-Intestinal Cancer Department, Mexico D.F., Mexico;* [2]*Oncology Hospital CMN "SXXI" IMSS, Translational Research Laboratory, Mexico D.F., Mexico;* [3]*INCan, Medical Oncology Department, Mexico D.F., Mexico;* [4]*INCan, Pathology Department, Mexico D.F., Mexico*

Background: Colorectal cancer (CRC) is the third most commonly diagnosed cancer worldwide. The aim of this study was to examine the interrelationship between the anatomical distribution of CRC by gender, age at presentation, and incidence rates for the disease in the National Cancer Institute of Mexico (INCan).
Material and Methods: A retrospective study was carried out on 403 cancer cases diagnosed in the Gastrointestinal Cancer Department of INCan, for a 6-year period (2004–2010). Data from clinical reports, computed tomography reports and surgical resection specimens were analyzed and included in a prospective database for statistical analysis. Tumours according colon-anatomy were classified as: proximal (PC), tranverse (TC), ascending (AC), descending (DC) and sigmoid colon (SC).
Results: Median age was 54 years (range 21−88 years). Distribution by gender was: 53.8% females and 46.2% males. Adenocarcinoma was the most frequent (94.9%) with moderately differentiated tumours predominantly. Twenty patients were identified as being in stage I (5%), 94 patients in stage II (23%), 132 patients in stage III (33%) 137 patients in stage IV (34%),15 patients were in recurrence (4%) and 1% (n = 5) of the patients were not classified. Colonic tumour localization was: 21.8% for PC (34%, stage I/II); 24.2% for TC (37%, stage IV), 46.6% for DC (38.2%, stage III) and 7.4% SC (53.3% stage II, III). Ninety-two (22.8%) of all cases were young patients (⩽40 years). Colonic tumour location compared with age was: young patients (⩽40 years) were mostly localized at DC (10.1%; and 31% stage IV) follow by PC (6.4%; and 46% in stage IV), and TC (4.9%). Meanwhile for patients over 40 years (77.2%), colonic tumour localizations predominantly were DC (36.4%), TC (19.1%) and AC

(15.3%). All patients where chemotherapy treated plus surgery, except for 38 patients (9.4%) who received best supportive care because of poor performance status (6 patients were ⩽40 years).
Conclusion: More than fifty percent of patients were diagnosed to have distal cancers. We found a large proportion (67%) of patients presented in advanced stages (III/IV), even in young people (⩽40 years). We show evidence about that increasing prevalence of CRC in young patients (22.8%). About colonic tumour location was interesting that 21.8% of cases were PC. These findings have important implications for CRC screening strategies, preventive and early detection programs in Mexico.

6033 POSTER

Ultra Low Anterior Resection for Distal Rectal Cancer − the End of the 1CM Rule?

W. Ceelen[1], Y. Van Nieuwenhove[1], D. Vande Putte[1], P.J. Elshout[1], P. Pattyn[1]. [1]*UZ University Hospital Gent, Surgery, Gent, Belgium*

Introduction: Controvery persists concerning the oncological safety of very close distal margins in patients with low (⩽5 cm) rectal cancer treated with neoadjuvant chemoradiation (nCRT).
Methods: All patients with low rectal cancer treated with nCRT (45 Gy) followed by sphincter saving surgery were identified from a prospective database. We analysed pathological and surgical outcome including local recurrence rate. Also, we studied the influence of distal margin (>1 cm versus ⩽1 cm) on overall survival using log rank analysis. Data are expressed as mean±SD or median (range).
Results: From 1998 until 2010, 109 patients (73% male) were identified. Clinically, 59% were staged as node positive. The pre-CRT distance from the anal verge was 3 cm (0.3−6). All patients underwent ultra low anterior resection; 35% underwent intersphincteric resection and colo-anal anastomosis. A protective ileostomy was constructed in 90% of patients. Stage distribution was as follows: stage 0 (ypCR): 16%, stage I, 30%, stage II, 21% and stage III, 19%. The median distal margin was 10 mm (0.1−40 mm). After a median follow up of 33 months, isolated local recurrence developed in 2 patients (1.8%) one of whom underwent successful surgical salvage. Two patients (1.8%) developed local and distant recurrence, while metastatic disease only developed in 25 patients (23%). Overall 5 year survival was 70%, and did not differ between a distal margin >1 cm versus ⩽1 cm (P = 0.18, log rank).
Conclusions: In patients with low rectal cancer undergoing nCRT, a distal margin <1 cm does not compromise local control or survival.

6034 POSTER

Hypoxic Antiblastic Stop-flow Pelvic Perfusion − a Step in the Therapeutic Flow-chart of Recurrent Colorectal Cancer

A. Ferro[1], P. Pilati[1], D. Miotto[2], E. Tessari[1], E. Mammano[1], D. Nitti[1]. [1]*Clinica Chirurgica II − Padova, Department of Surgical and Oncological Sciences, Padova, Italy;* [2]*Radiology Institute, University of Padova, Padova, Italy*

Background: Hypoxic antiblastic stop-flow perfusion (SFP) is a palliative locoregional treatment for patients with locally advanced inoperable tumours, based on the perfusion of the tumour's anatomic district after blood supply blockage achieved by means of intravascular inflatable balloon catheters.
Material and Methods: 26 patients affected by locally recurrent unresectable colorectal cancer were treated with a total of 43 pelvic SFP. All patients had received other previous treatments: surgery (26), systemic CT (23), RT (24), a previous pelvic SFP (11), two previous pelvic SFP (5) and previous three (1). Drugs delivered were a combination of Oxaliplatin and Mitomicin-C . Systemic and locoregional toxicity, tumour response, local progression-free survival and pain control rates were recorded. In cases of partial response or stable disease following the first SFP, a second or further procedures were taken into consideration if no distant metastases were found.
Results: A single SFP was performed in 32 patients; 6, 4 and 1 patient underwent respectively 2, 3 and 4 cycles of SFPs. The mean interval between repeated SFPs was 8 weeks (range 6−10 weeks). The mean hospital stay was 5 days (range 3−23 days).
No postoperative deaths occurred. Four methodical complications were recorded: 2 bleedings from the puncture site, 1 haematoma, 1 deep venous thrombosis and 1 artero-venous fistula. Mild locoregional and systemic toxicity were observed after 5 (12%) and 6 (14%) treatments. The mean drug leakage rate was 54%. Complete and partial response was observed in 2 (8%) and 8 (31%) patients, respectively (overall response rate = 39%). In these patients surgery was reconsidered. In 9 patients (35%) stabilization of disease was observed after one treatment. Median local progression free survival was 7 months (range 2−23 months). Median overall survival was 15 months: the higher the number of SFPs pursued per patient, the higher the overall survival. A high rate of pain control was achieved: 60% of patients decreased the dosages of pain-relievers,4 0% didn't use drugs anymore.
Conclusions: SFP is a semi-invasive procedure that shows encouraging results not only in terms of cancer related symptoms palliation, but surprisingly in terms of tumour response rates. Therefore indications to SFP should be extended as an alternative to the failure of traditional approaches and as a neo-adjuvant treatment to make surgical resection feasible.

6035 POSTER

Characteristics of Individuals With High Scores in the Model $PREMM_{1,2}$ Risk Assessment of Germline Mutations in MLH1 and MSH2

C. Guillen-Ponce[1], M.J. Molina-Garrido[2], M. Goicoechea[3], D. Salas[3], A. Carrato[1]. [1]*Hospital Ramón y Cajal, Medical Oncology, Madrid, Spain;* [2]*Hospital Virgen de la Luz, Medical Oncology, Cuenca, Spain;* [3]*Dirección de Salud Pública, Oficina del Plan del Cáncer, Valencia, Spain*

Introduction: Lynch syndrome is the most common inherited cause of colorectal cancer and is due to germline mutations in mismatch repair of errors of DNA base pairing (MMR genes). Most mutations occur in genes MLH1 and MSH2. The $PREMM_{1,2}$ model predicts the likelihood of being a carrier of a mutation in the genes MLH1 and MSH2 based on personal and family history of colorectal cancer and adenomas.
Material and Methods: From 2005–2008 124 genetic studies were carried out on patients with suspected Lynch syndrome; in 87 cases MLH1 and MSH2 were analyzed. Of these patients 20 were carriers of a MLH1 mutation (6) or MSH2 (14). Retrospectively, the $PREMM_{1,2}$ predictive model was applied to all individuals. We analyzed the sensitivity and specificity for different cutoff points. In individuals with higher $PREMM_{1,2}$ scores (⩾20%) personal clinical characteristics (sex, age at cancer diagnosis, tumour type, location, multiple tumours, presence of adenomas) and family (age of first cancer in the family, presence or absence of first-and second-degree relative with colorectal cancer and endometrial cancer) and diagnostic criteria (Amsterdam or Bethesda modified) were evaluated. Individuals with $PREMM_{1,2}$ ⩾20% were stratified according to whether or not they had MMR deficiency (microsatellite instability [IMS] or loss of expression by immunohistochemistry [IHC] of MMR proteins).
Results: 20 pathogenic mutations (22.98%) were detected: 6 of gene MLH1 and 14 MSH2. The cutoff of $PREMM_{1,2}$ influenced the ability to discriminate between carriers and non-carriers of mutation: for a cutoff of ⩾ 5% the sensitivity was 100% and specificity of 14.9% and mean positive predictive (PPV) of 25.9%; for a cutoff of ⩾ 20% the sensitivity fell to 71.64% while the specificity increased to 45%, and PPV was 32.14%. There were 28 individuals who scored ⩾ 20%. In 27 of these the MMR status was known. There were no differences in any personal or familial clinical features among the 16 patients with MMR deficiency and 11 without MMR deficiency, except in the type of cancer: all individuals who scored ⩾ 20% and did not have MMR deficit were suffering from colorectal cancer, whereas in the MMR-deficient group there were 6 individuals with extracolic tumours (5 endometrial cancers and 1 stomach cancer) (p = 0.046).
Conclusions: The discriminative capacity of the $PREMM_{1,2}$ model varies according to different cutoff points. The $PREMM_{1,2}$ score in combination with MMR status identifies a subset of patients who differ in the type of tumour present. Colorectal cancer is the only type of tumour diagnosed in individuals with $PREMM_{1,2}$ ⩾20% with tumours without MMR deficiency.

6036 POSTER

Non-specialist Decision Making in the Management of Metastatic Colorectal Cancer

R. Jones[1], S. Fenwick[1], G. Poston[1], D. Berry[2], D. Dunne[1], H. Malik[1]. [1]*University Hospital Aintree NHS Foundation Trust, Department of Hepatobiliary Surgery, Liverpool, United Kingdom;* [2]*University of Leicester, Department of Hepatobiliary Surgery, Leicester, United Kingdom*

Background: Improved surgical techniques and chemotherapeutic regimens have meant that the definition of resectable metastatic liver disease is evolving. UK NICE guidance 176 implies that all patients with liver-only metastatic colorectal cancer should have their treatment managed by an MDT with access to specialist liver surgeons.
This study aimed to assess local colorectal MDT decision-making on resectability of liver-only metastatic colorectal cancer.
Methods: All pattients treated with palliative chemotherapy between January and December 2009 at a regional oncology unit for metastatic colorectal cancer were identified using a prospectively maintained database. This was then cross-referenced with the regional hepatobiliary multidisciplinary database, to identify patients who had been discussed with a liver surgeon. Imaging for all patients who had not been reviewed by a liver surgeon was retrieved. Patients with disseminated malignancy were excluded, leaving a cohort of patients with liver only metastatic