6156 POSTER

Noninvasive Measurements From Computed Tomography and Laboratory Results Predict Hepatic Sinusoidal Injury Associated With Oxaliplatin-based Chemotherapy in Patients With Metastatic Colorectal Cancer

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Purpose: In patients (pts) with metastatic colorectal cancer (mCRC), sinusoidal obstruction syndrome (SOS) often results from oxaliplatin-based chemotherapy and is significantly associated with morbidities including treatment delay and hepatic dysfunction. Although liver biopsy is definitive in diagnosis of SOS, it is invasive. We have planned this study to investigate noninvasive parameters to predict SOS in mCRC pts with oxaliplatin-based chemotherapy.
Patients and Methods: Thirty-nine mCRC pts were prospectively accrued for 1st line chemotherapy of oxaliplatin plus oral fluoropyrimidines (S-1 or capecitabine). Serial measurements of 3 noninvasive parameters were performed; liver index (LI), splenic volume (SV) and aspartate aminotransferase to platelet ratio index (APRI). Based on CT imaging, LI was calculated by multifocal measurement of housefield units (HU) of liver (L), portal vein (P) and aorta (A) to represent both hepatic parenchyme and sinusoidal blood (LI = [L − 0.3(0.75P + 0.24A)]/0.7) and SV measured using sum of disks methods. APRI was calculated by [(measured serum AST/normal serum AST)/blood platelet count (10^9/L)]*100. Mixed linear models were used to assess the correlations between oxaliplatin cumulative doses and changes of LI, SV and APRI.
Results: After treatment of oxaliplatin-based chemotherapy (cumulative doses: median 920 mg/m^2), median decrement of LI, increments of SV and APRI was 26.6 HU (range, −4−75), 99 ml (range, −13.8–317.2 ml), and 0.64 (range, 0.05–1.83), respectively. Increased oxaliplatin cumulative doses were statistically correlated with decreased LI (t-value = −7.998, $p < 0.001$), increased SV (t-value = 9.889, $p < 0.001$) and increased APRI (t-value = 11.467, $p < 0.001$).
Conclusion: Noninvasive measurements of LI and SV from conventional CT scans and APRI from routine laboratory results can be used as surrogate markers for hepatic sinusoidal injury, and can be easily performed without additional invasive procedures.

Table: Multivariable-adjusted association between candidates of surrogate markers and oxaliplatin cumulative dose

Dependent variable	Association with oxaliplatin cumulative dose			
	β[a]	Standard error	t-value	*p*-value
LI	−0.001	<0.001	−7.998	<0.001
SV	0.001	<0.001	9.889	<0.001
APRI	0.002	<0.001	11.467	<0.001

[a]β was estimated by using a mixed linear models adjusted for age, sex, chemotherapy regimen, diabetes and body mass index.

6157 POSTER

Use of Aspirin Postdiagnosis Improves Survival for Colon Cancer Patients

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Background: It is not clear whether aspirin use can influence the prognosis of patients diagnosed with colorectal cancer (CRC). In animal models, aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs) have shown to inhibit tumour growth and metastases as well as prolong survival. Aim of the present study was to assess survival according to aspirin or other non-aspirin NSAIDs use before and after the diagnosis of CRC.
Methods: Data were obtained from the Dutch PHARMO record linkage systems and the Eindhoven Cancer Registry. From these databases, a total of 4481 patients diagnosed with CRC were identified in the period 1998–2007. Aspirin and NSAID use was defined as none, prediagnosis & postdiagnosis and only postdiagnosis use. Overall Survival was calculated with the status of user or nonuser as time-varying covariate by the method of episode splitting. Patients were coded as nonuser in the time from diagnosis to first use and as user in the period from first use to the end of follow-up.
Results: In total, 1176 (26%) patients were defined as nonusers, 2086 (47%) prediagnosis & postdiagnosis users and 1219 (27%) only postdiagnosis users. In all colon cancer patients the adjusted Rate Ratio (RR) for Overall Survival in users of aspirin/NSAIDs postdiagnosis as compared to nonusers was 1.60 (95% CI 1.37–1.86; $p < 0.001$). However for aspirin users (initiated postdiagnosis) the adjusted RR was 0.72 (95% CI 0.56–0.93; $p = 0.01$). For frequent users of aspirin (more than 3 prescriptions) the effect was larger (RR 0.68 (95% CI 0.51–0.89; $p = 0.005$). For rectal cancer patients no significant survival gain for NSAIDs or aspirin was observed in users as compared to nonusers.
Conclusion: Only aspirin use initiated after the diagnosis of colon cancer is associated with an increased survival. Survival gain was even stronger for frequent users of aspirin.

6158 POSTER

Lack of Relationship Between CYP3A7*1C Polymorphism and Colorectal Carcinogenesis in Hungarian Population

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Background: The role of CYP3A7 enzyme is well known in the metabolism of steroid hormones. This enzyme is predominantly expressed in the foetal liver, and its expression seems to be silenced shortly after birth. However, in case of CYP3A7*1C mutant variant, the enzyme expression remains at a higher level with decreased levels of androstenedione, oestrone and oestrone sulphate as well. Based on the fact, that oestrogen in forms of oral contraceptives or postmenopausal supplementation was shown to reduce the risk for colorectal cancers, we hypothesized that the occurrence of CYP3A7*1C variant, through the altered steroid hormone profile, has a deteriorating effect on colorectal carcinogenesis.
Material and Methods: We collected 538 participants, 278 subjects (130 female and 148 male) with colorectal adenocarcinoma and 260 healthy blood donors. The age at the time of the diagnosis was 61±11 years. Median follow-up period was 17 months (range 1−20 months). Within the follow-up period, 58 patients experienced disease recurrence, the majority (n = 44; 76%) of them developed distant metastases. Markers of tumour progression (CEA, AFP, CA19-9) were measured. Genetic investigation of CYP3A7*1C (rs11568825) was carried out by restriction fragment length polymorphism.
Results: Mutant allele frequencies were the same in the patient and in the control group with 3%, but homozygous mutant GG genotype was found among the control participants. CYP3A7-*1C genotypes did not relate to the incidence of colorectal cancer (OR = 1.21; 95% CI = 0.57–2.57; $p = 0.626$) nor to the number of distant recurrences (OR = 0.74; 95% CI = 0.19–2.85; $p = 0.664$). Neither survival parameters (for DFS log rank test $p = 0.39$; for OS log rank test $p = 0.12$), nor tumour marker levels (for CEA $p = 0.39$; for AFP $p = 0.10$; for CA19-9 $p = 0.31$) did show any significant differences among the genotypes.
Conclusions: The CYP3A7*1C polymorphism did not have any significant effects on colorectal carcinogenesis. Findings from previous studies on prostate and breast cancer also failed to prove any relationship with this genetic variant suggesting the existence of a more complex regulation in the case of these tumours.

6159 POSTER

Quality of Life and Stress in Patients With Colorectal Cancer Before Starting Chemotherapy

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Background: According to transactional theory stress occurs when a person has to use all the resources he owns and cannot cope successfully with the situation. The difference between perceived request of resources and possible responses of the same contributes to forming stress and consequently impacts Individual's health. Because of this, several research studies have been developed finding a relationship between perceived stress and quality of life (QoL); but little has been described about stress

in patients with colorectal cancer and its relationship with QoL, particularity with chemotherapy described as one important stressor. Therefore the main aim of this study was to explore the relationship between stress and QoL in patients who received chemotherapy for the first time.
Material and Methods: The sample was integrated by 27 colorectal cancer patients; 13 women and 14 men, whose ages were between 24 and 70 years old. After medical oncologist consultation, where chemotherapy treatment was assigned for the first time, participants were recruited; those who accepted to participate in the study signed an informed consent form and were referred for a comprehensive assessment session.
The Perceived stress scale (PSS) utilized measures the level of stress control perceived, the Health Related Quality of Life Inventory (InCaViSa) measures QoL in chronic or acute diseases; The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) measures QoL in patients with cancer. All instruments have appropriate psychometric properties for Mexican population.
Results: According to PSS, 45% of patients showed low levels of stress, 48% moderate and 7% high levels of stress. A significative negative correlation was found with stress perception and physical performance, cognitive functioning, free time and daily life evaluated by InCaViSa scale. A significative positive correlation was found with stress perception and fatigue, pain, insomnia and financial difficulties scales. Finally, a significative negative correlation was found with physical, role, emotional, cognitive and social functioning and with the global QoL evaluated by EORTC QLQ-C30.
Conclusions: In general terms, higher levels of stress were observed when higher level of simtomatology and problems like fatigue, pain, insomnia and financial difficulties were reported, and also less functionality in physical, role, emotional, cognitive and social domains, including physical performance, free time and daily life, all of which traduced in worst QoL in patients with colorectal cancer before receiving chemotherapy for first time.

6160 POSTER

Impact of Adjuvant Chemotherapy on Survival of Patients With Stage II Colon Cancer − Retrospective Study

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Background: Colorectal cancer (CRC) is the third most common malignant tumour. The stage of the tumour at time of resection is the most important prognostic factor. The issue of adjuvant treatment for stage II colon cancer patients using 5-FU-based therapy is less well defined, But; the clearly well established survival benefit for stage III colon cancer patients have led some physicians to recommend adjuvant chemotherapy for stage II colon cancer patients.
Materials and Methods: This retrospective study was conducted on all pathologically confirmed stage II colon cancer patients (273 patients) who received adjuvant chemotherapy in the Clinical Oncology Unit, Radiation Sciences Department, Medical Research Institute, Alexandria University between January 1995 to December 2004. The data including: Clinicopathological Parameters (Age, Sex, Family history, Tumour histology, Tumour grade, Tumour marker, Number of lymph nodes dissected, Vascular invasion and Bowel obstruction) Adjuvant Chemotherapy in the form of 5-FU+Ca leucovorin (Regimens of chemotherapy received either Mayo clinic or De Gramont regimen), Doses of chemotherapy and Number of cycles were registered.
Results: More dissected lymph nodes were accompanied by higher disease-free survival (DFS) and overall survival (OS) rates at 3 and 5 years respectively; but did not reach statistical significance. Patients who had symptoms duration less than 6 months (earlier presentation) had statistically significant higher OS at 3 years but not at 5 years. Symptoms duration showed no impact on DFS. There was no difference in DFS and OS in different systemic chemotherapy regimens. Patients who received 6 cycles had significant higher DFS when compared with patients who received less number of treatment cycles. Intestinal obstruction was accompanied by lower OS at 3 and 5 years and DFS at 3 years only. Vascular invasion had impact on both DFS and OS at 3 and 5 years. Higher level of CEA was accompanied by lower DFS and OS at 3 and 5 years. Patients who had poorly differentiated tumours had lower DFS when compared with patients who had well differentiated tumours. For all patients, DFS at 3 & 5 years were (72.9%) and (57.1%) respectively, while OS at 3 & 5 years were (86.1%) and (73.6%) respectively.
Conclusion: Although there was no improvement in OS, DFS was significantly better with adjuvant chemotherapy. Stage II colon cancer patients who have high risk features, including intestinal obstruction, vascular invasion, inadequate lymph node dissection or T4 disease seem to benefit from adjuvant systemic chemotherapy. The co-morbidities and likelihood of tolerating adjuvant systemic chemotherapy should be considered as well. Also, researchers must continue to search for other therapies which might be more effective, shorter in duration and less toxic than those available today.

6161 POSTER

Hardly Any Excess Mortality for Long-term Colon Cancer Survivors in the Netherlands 1989–2008

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Background: With the marked increase in the number of long-term cancer survivors, there is an increasing need for more up-to-date analysis of survival for patients who have already survived a certain period of time. Standard survival curves at diagnosis of cancer are rather pessimistic, since they are also based on patients who die within the first few years. Conditional 5-year relative survival therefore serves better information about the current prognosis of survivors during follow-up. We determined conditional 5-year relative survival rates for colon cancer patients, according to age, gender, and tumour stage for each additional year survived up to 15 years after diagnosis.
Methods: Patients diagnosed in the Netherlands with colon cancer stage I−III in 1989–2008 aged 15−89 years were selected from the Netherlands Cancer Registry. Conditional 5-year relative survival was computed for every additional year survived up to 15 years. Period analysis with follow-up period 2004–2009 was used.
Results: There was hardly any excess mortality (conditional 5-year relative survival >95%) 1−4 years after diagnosis for stage I patients and 4−7 years after diagnosis for stage II patients, with patients aged 45−74 years reaching this point later compared to the younger and elderly patients. For stage III patients, hardly any excess mortality was observed 5 years after diagnosis for those aged 75−89 years, but remained elevated up to 13 years after diagnosis for those aged 15−44 years. Initial differences in relative survival at diagnosis between age and stage groups largely disappeared with number of years survived.
Conclusion: The prognosis for colon cancer survivors improved with each additional year survived. In the first years after diagnosis conditional survival improved largely for all colon cancer patients, especially for stage III patients. There was hardly any excess mortality for colon cancer patients stage I-III at some point within 15 years after diagnosis, being later for more advanced stage. Quantitative insight into conditional survival for cancer patients is useful for caregivers to help planning optimal cancer surveillance and inform patients about their prognosis.

6162 POSTER

Incidence of Major Surgeries in Patients With Metastatic Colorectal Cancer

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Background: As surgical procedures may potentially interfere with anticancer drug therapy for metastatic colorectal cancer (mCRC), the objective of this study was to examine the proportion of patients with mCRC who underwent major surgeries.
Methods: Using a large U.S. medical claims database from a nationally commercially-insured population, patients with diagnosed mCRC between January 2004 and March 2010 were identified. The first metastasis diagnosis date served as the index date. Patients were followed from the index date to death, disenrollment, or end of the study period (March 31, 2010), whichever occurred first. Major surgery was defined according to the list of major surgeries developed by the National Committee for Quality Assurance (NCQA) using Current Procedural Terminology (CPT) procedure codes. Major surgeries were examined by anatomic locations: 1) colon or rectum; 2) liver or lung; and 3) all other anatomic sites. Major surgeries on colon or rectum were assessed separately, since they likely include a high percentage of interventions to remove primary tumours. The proportion of major surgeries was descriptively analyzed.
Results: The study sample included 4,768 mCRC patients who met the study inclusion and exclusion criteria between January 2004 and March 2010. Mean age was 60.0 years old and 45.9% of patients were female. Mean length of follow-up observation period was over one year (414 days). Overall, 42.3% of patients had at least one major surgery on anatomic