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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.

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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.

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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.

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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