INTRODUCTION: Liver cancer occurs in approximately 1% of Poles affected by all cancers. In 2010 its standardised incidence rate amounted to 2.9/100 thousand for males and 1.4/100 thousand for females.
AIMS&METHODS: The aim of the study was to identify the dietary factors, which could contribute to trends in liver cancer morbidity in Poland.
Standardised liver cancer incidence rates according to gender were derived from the National Cancer Registry. The information source on the dietary trends was data derived from the national food balance sheets showing food quantities available for consumption per capita/year. The Spearman rank correlation coefficient was used as a measure of the relationship between examined variables. Dietary variables included the consumption of fruit, cereals (as potential source of aflatoxins) and alcohol.
RESULTS: High adverse correlations were found for liver cancer incidence rates and fruit consumption, (-0.69 for males and -0.64 for females). Fruit consumption significantly increased in studied period – from 37.7 to 55.5 kg. Positive correlations (0.45 for men and 0.57 for women) were noted with respect to cereals consumption, which decreased from 130.2 to 110.0 kg.
Obtained results do not indicate positive correlations between liver cancer incidence rates and alcohol consumption. However in the in the early 80's an important decline in alcohol consumption was noted and could contribute to later decrease in liver cancer morbidity.
CONCLUSION: It seems that the trends in liver cancer incidence rates in 1980-2010 in Poland were affected by the growing fruit consumption. The decline in cereals consumption could play a protective role also. Improvement of cereal grains storage and implementation of food quality systems into cereal production could lead to decline in aflatoxins content in grains and thus strengthen this protective effect.
It is difficult to determine the influence of alcohol consumption on liver cancer morbidity. It is not unlikely that downward trends observed since beginning of the 90's were affected among others by earlier decline in alcohol consumption, but statistical analysis did not confirm it.
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Disclosure of Interest: None Declared
Keywords: cancer, diet, liver

P1187 SERUM ENDOCAN AS A NOVEL PROGNOSTIC BIOMARKER IN HEPATOCELLULAR CARCINOMA PATIENTS

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INTRODUCTION: Endocan is a vascular endothelium-derived factor regulated by angiogenic factors. Recent studies have shown that endocan is overexpressed at the mRNA and/or protein levels in various types of tumours.
AIMS&METHODS: We examined whether serum endocan can be a prognostic biomarker for survival in hepatocellular carcinoma (HCC) patients. Serum endocan levels were measured for 64 naïve HCC patients (median age 71 years, male 41; female 23) and 15 non-HCC subjects. Prognostic factors for survival were investigated by univariate and multivariate analyses using the Cox proportional hazard model. The following variables recoded into binary categories were assessed as potential prognostic factors: age (<70 years vs. ≥ 70 years), gender (female vs. male), etiology of liver disease (non-viral vs. viral), tumour stage (stage I/II vs. III/IV), Child-Pugh grade (A vs. B/C), treatment option (curative vs. non-curative), serum endocan (<2.20 ng/mL vs. ≥ 2.20 ng/mL), serumα-fetoprotein (AFP) (<100 ng/mL vs. ≥ 100 ng/mL) and serum des-γ-carboxy prothrombin (DCP) (<26 mAU/mL vs. ≥ 26 mAU/mL). The overall survival rates were calculated using Kaplan–Meier analysis, and the differences were evaluated by the log-rank test.
RESULTS: Serum endocan levels were 3.73 (0.74–10.95) ng/mL in HCC patients and 1.25 (0.93–3.54) ng/mL in non-HCC subjects, respectively ($P = 0.0002$). Elevated serum endocan levels were significantly associated with poor hepatic function ($P = 0.015$), a higher number of tumours ($P = 0.034$) and presence of vascular invasion of HCC ($P = 0.043$). During a median follow-up period of 23.0 months, 33 patients died due to the following causes: HCC in 23 patients, hepatic failure in 7 patients, other diseases in 2 patients and unknown cause in 1 patient. The cumulative overall survival rates were 78.8%, 56.5% and 37.9% at 1, 3 and 5 years, respectively. On multivariate analysis, elevated serum endocan levels, as well as elevated serum AFP and DCP levels, were significantly associated with poor survival (hazard ratio 2.36, 95% confidence interval 1.22–5.36, $P = 0.008$). When combining serum endocan and tumour markers, increase in number of elevated markers provided a worse survival ($P < 0.0001$).
CONCLUSION: Serum endocan may be a promising prognostic biomarker for survival in HCC patients. The combined use of serum endocan with serum AFP and DCP can allow a better prognostic stratification for such patients.
Disclosure of Interest: None Declared
Keywords: Endocan, Hepatocelluar carcinoma, Prognostic Value

P1188 CANCER-STEM CELL-LIKE SPHERE CELLS INDUCED FROM A CELL LINE DERIVED FROM POORLY-DIFFERENTIATED HEPATOCELLULAR CARCINOMA EXERTS LIVER METASTATIC POTENTIAL AND CHEMORESISTANCE

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INTRODUCTION: It is thought that cancer-stem cell (CSC) plays important roles in carcinogenesis, recurrence, metastasis, and chemoresistance. Recently, it was suggested that the possible existence of plasticity between CSCs and their more differentiated derivative cancer cells. We hypothesized that poorly-differentiated hepatocellular carcinoma (HCC) has potential that convert to CSC, which would responsible for metastasis and recurrence.
AIMS&METHODS: Human HCC cell lines, SK-HEP-1, HLE, HuH-7, and Hep 3B, were used for sphere induction. Sphere induction was accomplished by using specified medium based on the medium for neural stem cells. Liver metastatic potential was examined by injection of the cells to immune-deficient mice spleen. Cell viability was measured by MTS assay. 9 anti-cancer agents (5-Fluorouracil, Cisplatin, Carboplatin, Docetaxel, Doxorubicin, SAHA, Irinotecan, Sorafenib, Sunitinib) were used. The mRNA and protein levels were examined by real-time PCR and flow cytometry analyses. ALDH activity was measured by ALDEFLUOR assay. Reactive oxygen species (ROS) activity was measured with the cell-permeable fluorogenic probe, 2', 7'-Dichlorodihydrofluorescin diacetate.
RESULTS: A cell line derived from poorly-differentiated HCC, SK-HEP-1, formed Sphere, although cell lines derived from well-differentiated HCCs, HuH-7 and Hep 3B, could not form sphere. Sphere cells induced from SK-HEP-1 cells (SK-sphere) showed higher mRNA levels of NANOG, LIN28A, and ABC transporters and ALDH activity compared to SK-HEP-1 cells. SK-sphere cells also showed increased liver metastatic potential compared to parental cells. SK-sphere cells represented obvious decreased-sensitivity to 5-Fluorouracil, Docetaxel, Doxorubicin, and SAHA. Sorafenib was effective in both SK-HEP-1 and SK-sphere cells. SK-sphere cells showed induced P21 mRNA and cell cycle arrest in G0/G1 phase. The ROS activity in SK-sphere cells was lower than those in SK-HEP-1 cells. On the other hand, the HIF1-alpha expression in SK-sphere cells was higher than those in SK-HEP-1 cells. Increased expression of Vimentine and decreased expression of EpCAM were observed in SK-sphere cells compared to parental cells. Higher SNAI1 mRNA level of SK-sphere cells was also observed.
CONCLUSION: Our induced sphere cells, SK-sphere, showed increased metastatic potential, chemoresistace, and epithelial-mesenchymal transition.
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Disclosure of Interest: None Declared
Keywords: cancer stem cell, chemoresistance, hepatocellular carcinoma, recurrence

P1189 MOLECULAR INVESTIGATIONS BY RAMAN IMAGING FOR A RELIABLE DIAGNOSIS OF HEPATOCELLULAR CARCINOMA

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INTRODUCTION: Patients with hepatocellular carcinoma (HCC) can only be treated curatively at early stages thus providing a favorable prognosis of this often fatal disease. However, histopathological examinations of different liver lesions remain a challenge for pathologists. Because of its high information content Raman spectroscopy is particularly suitable for investigating cellular and subcellular constituents. By using recognition and classification algorithms tissue-specific patterns can be discovered in order to develop an independent model for secure HCC prediction.
AIMS&METHODS: The aim of the present study is to investigate molecular information about HCC and non-malignant liver tissue by Raman imaging in order to use the obtained spectral patterns for diagnosis.
Human hepatic tissue sections were measured with the confocal Raman microscope. A parallel section of each sample was stained with HE to assign tissue regions to HCC (n=12), fibrotic tissue (n=14) and regenerative nodules (n=4). Raman spectra were acquired and the average and difference spectra of each region were calculated. A training data set including the spectral data from regions of HCC (n=6) and fibrosis (n=7) were used to generate a classification model based on a support vector machine algorithm. The obtained classifier was applied to independent validation data sets of HCC regions (n=6) together with regions of fibrosis (n=7) and the same HCC regions (n=6) together with regenerative nodules (n=4).
RESULTS: Analyzing the difference spectra of malignant and non-malignant tissue, distinct spectral differences in the negative bands at 1676, 1387, 1345, 1241, and 936 cm^{-1} and in the positive bands at 1739, 1653, 1436, 1300, 1076, 890, and 721 cm^{-1} were identified. The classification model based on the training data set calculated a prediction accuracy of the classification model of 81%. The developed classifier was able to predict previously unknown HCC and fibrotic tissue with an accuracy of 90% (sensitivity 78%, specificity 100%). The performance of the same classification model to predict regions of HCC and regenerative nodules resulted in an accuracy of 82% (sensitivity 72%, specificity 83%).
CONCLUSION: In this study Raman imaging spectroscopy was for the first time applied successfully to tissue of the cirrhotic liver with the aim to differentiate, classify and predict with high accuracy malignant and non-malignant tissue regions. The demonstrated results highlight the enormous potential which light scattering techniques have for future diagnostics of cancer.
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Disclosure of Interest: None Declared
Keywords: Classification model, Fibrosis, Hepatocellular cancinoma, Prediction, Raman imaging, Regenerative nodules