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Non-Invited Publications

Hepatobiliary Cancer

01 SCIENTIFIC POSTER ABSTRACT

The risk level of liver cancer cases among smokers in developing countries

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Introduction: Tobacco use is a rising concern for the developing world. It causes about 5 million deaths yearly and is projected to cause 10 million deaths yearly by 2025 with 80% of these deaths from the developing countries if current trends continue. Tobacco is also a major risk factor for all kinds of cancer including Liver cancer.
Goal: To help determine whether the risk of liver cancer from smoking was less or greater than other forms of cancers caused by tobacco.
Methods: In this study, we ascertained retrospectively the smoking habits of 24,000 adults who had died from liver cancer (cases) in 10 Chines cities, 7 Indian Cities and 5 Nigerian Cities. These areas were chosen for reasons of high population. Smokers from these three countries constitute 40% of smokers worldwide. Calculations of the smoker risk ratios (RR) for liver cancer mortality were standardized for age and locality. We used Cox proportional hazard regression models to adjust for confounding variables. We conducted analysis on the entire study population, among male and females who had smoked for at least 20 years separately for each country.
Results: Among adult men (aged 35+) there was a 36% excess risk of death from liver cancer (smoker standardized risk ratio [RR] = 1.36, with 95% confidence interval [CI] 1.29–1.43, $2p < 0.00001$; attributable fraction 18%). In the general male population, this indicates absolute risks of death from liver cancer before age 70 of about 4% in smokers (in the absence of other causes). The RR was approximately independent of age, was similar in urban and rural areas, was not significantly related to the age when smoking started but was significantly ($p < 0.001$) greater for cigarette smokers than for smokers of other forms of tobacco. Among men who smoked only cigarettes, the RR was significantly ($p < 0.001$ for trend) related to daily consumption, with a greater hazard among those who smoked 20/day (RR = 1.50, 95% CI 1.39–1.62) than among those who smoked fewer (mean 10/day: RR = 1.32, 95% CI 1.23–1.41). Smoking was also associated with a significant excess of liver cancer death in women (RR = 1.17, 95% CI 1.06–1.29, $2p = 0.003$; attributable fraction 3%), but fewer women (17%) than men (62%) were smokers, and their cigarette consumption per smoker was lower. Among women who smoked only cigarettes, there was a significantly greater hazard among those who smoked at least 20/day (mean 22/day: RR = 1.45, 95% CI 1.18–1.79) than among those who smoked fewer (mean 8/day: RR = 1.09, 95% CI 0.94–1.25).
Conclusion: This study goes to show that even though liver cancer from tobacco use kills about 200,000 people yearly in these three developing countries, the deaths from lung cancer (1.5 million yearly worldwide) is still higher than liver cancer deaths.

02 SCIENTIFIC POSTER ABSTRACT

miRNA network dysregulation in hepatocarcinogenesis

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Goals: Tumor growth is tightly associated with regular shifts in microRNA (miRNA) expression pattern. More than 50% of miRNA genes are located in fragile chromosomal regions that are susceptible to various damages during the carcinogenesis. Usually, expression of miRNAs miR-22, miR-29, miR-122a, miR-124, miR-126, miR-148, miR-152, miR-203, miR-223, miR-375 is down-regulated in hepatocellular carcinoma (HCC) cells whereas expression of miRNAs miR-19a/b, miR-21, miR-31, miR-20a, miR-106a, miR-125a, miR-221, miR-222, miR-224, miR-301, miR-454, miR-483−5p is up-regulated. This investigation aims to identify how abnormalities in miRNA network contribute to the hepatocarcinogenesis.
Methods: miRNA targets within gene transcripts were predicted in silico using TargetScan software.
Results: Down-regulated miRNAs miR-22 and miR-148/152 silence WNT1 gene. miR-223 targets transcripts of genes encoding proliferative signal pathway components RASA1 and E2F1. Transcript of another oncogene N-Ras carries sites of miR-22, miR-29, miR-124 and miR-148/152. miR-124 and miR-203 target transcript of gene encoding antiapoptotic pathway component Akt2. Also, miR-203 silences gene of transcription factor E2F3 as well as gene BIRC5 encoding survivin. miR-124 silences E2F3, E2F5, E2F6 genes as well as gene of cyclin-dependent kinase CDK4. miR-148/152 targets E2F3, E2F7, CDK6, CDK8 gene transcripts. miR-22, miR-29 and miR-122a silence gene LAMC1 encoding laminin g1. Also, miR-148/152 and miR-29 target LAMA4 and, respectively, LAMA2 and LAMC2 gene transcripts. Up-regulated miRNAs miR-221 and miR-222 silence genes encoding cell cycle inhibitors p27 and p57. miR-19 inhibits gene encoding tumor suppressor protein pTEN and thus derepresses PI-3K/Akt antiapoptotic signaling pathway. miR-20a as well as miR-106a target transcripts of genes encoding pTEN, cell cycle inhibitors p21 and Rb1. Also, transcript of gene encoding p21 carries miR-301/454 target.
Conclusion: miRNA network is intertwined with signal transduction pathways. HCC cells down-regulate expression of miRNAs that silence proliferative and antiapoptotic genes. Moreover, down-regulation of some miRNAs can allow the ectopic expression of laminins that are heteroorganic antigens. Up-regulated miRNAs suppress genes encoding cell cycle inhibitors. Therefore, shifts in miRNA expression pattern can themselves cause reactivation of cell oncogenes and antiapoptotic genes as well as repression of cell cycle inhibitor genes. Furthermore, as each miRNA impairs the expression of many genes, including genes of other miRNAs, illegitimate activation or repression of some miRNA genes can be the first event in carcinogenesis, leading to the reorganization of epigenetic pattern in transforming cells through the RNAi-dependent DNA methylation. As a result, cancer cells proliferate and accumulate, forming a tumor.

Gastric Cancer

03 SCIENTIFIC POSTER ABSTRACT

Extracapsular lymph node spread: not-so-well known but important prognostic factor in gastric cancer

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Goals: Current AJCC and JCGC pN staging system of gastric cancer are both based on the number of metastatic lymph nodes. Instead, little has been done about the histopathological characteristics of the metastatic lymph node itself, specially for the prognostic impact of tumor penetration through the nodal capsule in metastatic lymph nodes, also called extracapsular lymph node involvement. Aim of this study is to evaluate the significance of extracapsular lymph node involvement as a prognostic factor and its correlation with clinicopathological parameters.
Methods: We took account of 96 patients underwent curative gastrectomy for gastric adenocarcinoma. In the present study, number of metastatic lymph nodes with capsular and/or extracapsular lymph node involvement was also evaluated. Extracapsular lymph node involvement was defined as invasive cancer extending through the nodal capsule into the perinodal adipose tissue. The deposits of invasively growing cancer cells without a recognizable lymph node were considered extracapsular lymph node involvement, unless these deposits were associated with perineural and/or vessel involvement.
Results: Extracapsular lymph node involvement was associated with higher nodal status ($P = 0.037$), with higher TNM stages ($P < 0.001$).