O6 - Comunicación Oral/Oral communication

Cáncer I

Cancer I

Jueves 2 de Octubre / Thursday 2, October
11:30:00 a/to 13:30:00

Moderador/Chairperson:
Miquel Porta

041

CANCER SURVIVAL IN PARENTS WHO LOST A CHILD: A NATIONWIDE STUDY IN DENMARK

Jiong Li*, Christoffer Johansen**, Jørn Olsen*
**Danish Epidemiology Science Centre, Aarhus, Denmark. **Department of Psychosocial Cancer Research, Institute of Cancer Epidemiology/Danish Cancer Society, Copenhagen, Denmark.*

Introduction: Psychological stress has been suggested to shorten cancer survival but only few studies have examined the effect of parental bereavement, and the results have been inconsistent. This study is to investigate the effect of the death of a child on the overall and specific cancer survival in parents who lost a child.
Methods: We identified all 21,062 parents who lost a child in Denmark from 1980 to 1996. Among them, 1630 parents had a subsequent incident cancer and they were recruited to the exposed cohort. We recruited 6237 incident caner patients from a group of 293,745 randomly selected unexposed parents matched on family structure at the same time as the bereaved parents. All incident cancers in the two cohorts were followed to the end of 1997, or until they died. Cox's proportional-hazards regression models were used to evaluate the hazard ratio (HR) of dying in exposed parents with cancer. We studied survival for: All cancers, site-specific cancers, smoking-related cancers, alcohol-related cancers, virus/immune-related cancers, lymphatic/haematopoietic cancers, and hormone related cancers.
Results: The overall HR of dying from an incident cancer in exposed parents was 1.23 (95% CI 1.03-1.47), compared to parents with cancer who did not loose a child. The HRs were nearly identical to those in the unexposed parents for site-specific cancers like lung cancer, breast cancer and other groups of cancers like cancers in all digestive organs, smoking related cancers, alcohol related cancers, hormone-related cancers and virus/immune-related cancers, and lymphatic/haematopoietic cancers.
Conclusions: Death of a child is not a strong prognostic factor for cancer survival among parents diagnosed with cancer after the bereavement. However, a small impairment in overall cancer survival cannot be ruled out.

042

CLINICAL VALUE OF SEROLOGICAL MARKERS, INMUNOHISTOCHEMICAL MARKERS AND TOBACCO CONSUMPTION PREDICTING RELAPSE, METASTASIS AND DEATH IN NON-SMALL CELL LUNG CANCER

Marina Pollán, Nuria Aragonés, Gonzalo López-Abente, Beatriz Pérez-Gómez. En nombre del Grupo: Group: Prognostic Factors in NSCLC
Unidad de Epidemiología Ambiental y Cáncer, Centro Nacional de Epidemiología del ISCIII, Madrid, Spain.

Objective: To assess the prognostic value of p53 and c-erbB-2 immunostaining, preoperative serum levels of CEA and CA125 and tobacco consumption in non-small cell lung cancer (NSCLC) patients with resectable tumours.
Methods: A prospective cohort of 465 NSCLC patients who underwent complete surgical resection in 13 Spanish hospitals were followed-up for a minimum of two years until the end of the study. Smoking information was obtained through a structured questionnaire applied by non medical trained interviewers once the patient had been discharged from the hospital. The average consumption during the 5 years previous to diagnosis was considered as a possible prognostic factor. Four end-points were considered: lung cancer death, relapse in general, loco-regional relapse and metastasis development. Standard statistical survival methods, namely Kaplan-Meier and Cox regression, were used. For comparison porpouses, the same multivariate model was fitted for each end-point. To explore the discriminative power of the final model in early stages of lung cancer, a score constructed using the linear predictor from the final model was applied to the more homogeneous group of patients in stage IB (202 patients), given there were very few cases in stage IA.
Results: Pathological T and N classifications continue to be the strongest predictors regarding either relapse or mortality. However, three of the studied markers seemed to add further useful information, but in a more specific context. For example, increased CEA concentration defined a higher risk population among adenocarcinomas but not among people with squamous tumours; and p53 overexpression implied a worse prognosis mainly in patients with well differentiated tumours. The analysis of type of relapse proved to be very informative. Thus, CA125 level was associated with a worse prognosis mainly related with metastasis development. Another interesting result was the influence of smoking, which showed a clear dose-response relationship with the probability of metastasis. Applying the score from the final models to patients in stage IB it was possible to identify a subgroup of patients with a three-fold increased risk of metastasis development and death.
Conclusion: TNM is still the strongest predictor in NSCLC patients, but easily obtained markers can help to devise the best therapeutic decision. The role of tobacco seems to expand beyond etiology. The multidimensional nature of prognosis has been underinvestigated. As our results point out, the inclusion of a broader spectrum of end- points can be more informative.
Other Members of the Study Group (alphabetic order): Aurelio Arnedillo, Ricardo Arrabal, Emilio Canalís, Manuel Díez, Jorge Freixenet, Mauricio García, Javier García-Tirado, Ana Gómez, Guillermo Gómez, Rogelio González-Sarmiento, Dolores Ludeña, Joan Minguella, Dolores Ortega, Joaquín Pac, Juan José Rivas, Jose María Rojas, Fernando Sebastián, Mercedes de la Torre, Antonio Torres, Gonzalo Varela.

043

BLADDER CANCER: HIGHER RISK OF TUMOUR RECURRENCE IN WOMEN

Diana Puente[1], Núria Malats[1], Àlex Amorós[1], Adonina Tardón[2], Reina García-Closas[3], Consol Serra[4], Alfredo Carrato[5], Josep Lloreta[6], Lluís Cecchini[7], et al. En nombre del Grupo: for the EPICURO study group investigators
[1]Unitat de Recerca en Respiratòria i Ambiental, Instituto Municipal de Investigación Médica (IMIM), Barcelona, Spain. [2]Universidad de Oviedo, Oviedo, Spain. [3]Hospital Universitario La Laguna, Tenerife, Spain. [4]Consorci Hospitalari Parc Taulí, Sabadell, Spain. [5]Hospital General de Elche, Alicante, Spain. [6]Hospital del Mar, Barcelona, Spain. [7]Hospital Germans Trias i Pujol, Badalona, Spain.

Introduction: Contrarily to other cancers, the risk of dying is higher in women with bladder cancer than in men. Little is known about the risk of intermediate events (tumour recurrences and progression) in relationship to gender. Among the established prognostic factors for bladder cancer are invasiveness, nuclear grade, tumour size, multiplicity and the presence of carcinoma in situ, though it is not known whether these factors have the same effects in men and women.
Objective: The aim of the study is to assess whether the risk of bladder cancer recurrence is different for men and women.
Methodology: Patients (n=498) with superficial tumours newly diagnosed and recruited in 17 Spanish hospitals between May 1997 and April 2001 were included. Information on sociodemographics was collected through personal computer-assisted questionnaires. Clinical data related to diagnostic procedures, treatment and tumoral characteristics were collected from hospital records. Pathological characteristics of tumours were reviewed and reclassified according to WHO-ISUP'98 by an expert pathologist. Follow up information on tumour recurrence, progression, change of management and survival was gathered through hospital records and through direct personal telephone interviews. The Kaplan-Meier method and multivariate Cox regression were applied.
Results: Out of 498 cases, 108 developed tumoral recurrences (21% of men and 29% of women, p=0.133). Kaplan-Meier analysis showed that women tended to present more recurrences than men (p=0.100). The difference was statistically significant for a major subgroup of superficial tumours (TaGII) when the analysis was adjusted for potential confounders such as morphology and treatment (OR: 3.39 95%CI 1.23-9.39). A total of 42 cases presented tumoral progressions (8% in men and 10.6% in women, p=0.495). Women were not at a higher risk of progression than men after adjusting for confounding factors nor in any strata of the prognostic variables.
Conclusions: Overall, women presented a slightly increased risk of bladder tumour recurrence in comparison to men. The higher risk of recurrences in women was confined to TaGII tumours. Further investigation is needed to confirm this finding.
Partially funded by Fondo de Investigación Sanitaria 00/0745.

044

POOLED ANALYSIS OF CASE-CONTROL STUDIES ON FLUID INTAKE AND BLADDER CANCER

Cristina M. Villanueva Belmonte[1], Kenneth P. Cantor[2], Sylvaine Cordier [3], Jouni JK Jaakkola[4], Will D King[5], Charles F Lynch[6], Stefano Porru[7], Manolis Kogevinas[1].

[1]Respiratory and Environmental Research Unit, Institut Municipal d'Investigacio Medica, Barcelona, Spain. [2]Occupational Epidemiology Branch, US National Cancer Institute, Bethesda, USA. [3]U435, INSERM, Rennes, France. [4]Department of Public Health, University of Helsinki, Helsinki, Finland. [5]Deparment of Community Health and Epidemiology, Queen's University, Ontario, Canada. [6]Department of Epidemiology, University of Iowa, Iowa, USA. [7]Institute of Occupational Health, University of Brescia, Brescia, Italy.

Background: Prolonged exposure of the bladder urothelium to carcinogens in the urine has been suggested to affect the development of bladder cancer. In an attempt to clarify this hypothesis, epidemiological studies have evaluated the risk for bladder cancer in relation to quantity of fluid intake. Contrary to expectation, many studies found a slight excess risk in subjects with high total fluid intake, although results have not been consistent. We pooled and jointly analysed the data of the case-control studies of bladder cancer with detailed information on fluid intake and on contaminants of tap water, particularly disinfection by-products.
Methods: The pooled database includes two studies from USA, and one each from Canada, France, Italy and Finland, accounting for 3790 cases and 6075 controls. Inclusion criteria were availability of detailed exposure data and accessibility to original data. Primary data were combined using common definitions and coding schemes. Subjects under 30 and over 80 years old, and those with more than 2 years between diagnosis and interview were excluded. Total fluids, total tap water and total coffee intake were calculated. Average exposure to disinfection by-products (THMs-trihalomethanes) was estimated for 40 years prior to interview. Unconditional logistic regression was used and all odds ratios (OR) and 95% confidence intervals (95%CI) were adjusted for age, sex, centre, smoking status and ever worked in high-risk occupations.
Results: The average total fluid intake in the study population was 2.6 litres per day, with 1.5 litres from tap water. We found an overall increased risk for total fluid intake (OR per litre per day=1.08, 95%CI=1.03-1.12) and a dose-response pattern (OR for highest quartile=1.33, 1.16-1.53). OR were higher for total tap water intake (OR=1.16, 1.03-1.31) and a dose response pattern was also observed (OR for highest quartile=1.33, 1.13-1.57). Drinking more than 5 cups of coffee per day was associated with an increased risk (OR=1.28, 1.12-1.46). ORs increased with increasing levels of average THM exposure (OR for highest quartile 1.33, 1.15-1.53). Subjects in the highest quartile of tap water fluid intake and at the highest quartile of THMs had an OR of 2.3 relative to those in the lowest quartile at both. Exposure to disinfection by-products did not confound the ORs for fluid intake. ORs for total fluid and tap water were highest in men. All six studies found an excess risk for total fluid intake.
Conclusions: Our results strengthen the hypothesis that total fluid intake is associated with an increased risk of bladder cancer. There are no strong biological hypotheses explaining how high total fluid intake could increase the risk. The positive associations found in most epidemiological studies may be, in part, attributed to the types of fluid intake.

045

ROLE OF HEPATITIS C VIRUS INFECTION IN MALIGNANT LYMPHOMA IN SPAIN

Silvia de Sanjose[1], Alexandra Nieters[2], Jim J Goedert[3], Yolanda Benavente[4], Eva Domingo-Domench[4], Alberto Fernadez de Sevilla[5], Ramon Bosch[6], Pilar Herrera[7], Birgit Kalinowski[8], et al

[1]Epidemiologia i Registre del Cancer/ Viral Epidemiology, ICO/NCI, Barcelona/Spain, Rockville/USA. [2]Clinical Epidemiology German Cancer Research Center, Heilderberg, Germany. [3]Viral Epidemiology Branch, NCI, Rockville, USA. [4]Epidemiologia i Registre del Cancer, ICO, Barcelona, Spain. [5]Hematologia Oncologica, ICO, Barcelona, Spain. [6]Patologia, Hospital Verge de la Cinta, Tortosa, Spain. [7]Patologia, Ramon y Cajal, Madrid, Spain. [8]Internal Medicine IV, University Hospital of Heilderberg, Germany.

Background: Hepatitis C virus (HCV) has been implicated in the etiology of malignant lymphomas. We estimated the risk of lymphoma associated with detection of HCV infection.
Methods: Cases (N= 532) were consecutive patients newly diagnosed with a lymphoid malignancy between 1998 and 2002 in four centers in Spain. Lymphomas were diagnosed and classified using the WHO Classification. Controls (N=600) were hospitalized patients matched to the cases by 5-year age group, gender and study center. Several medical conditions associated with severe immunosuppression precluded the eligibility of controls. Patients underwent a personal interview and blood sampling. HCV positive subjects were considered those with antibody response to third generation ELISA and/or detection of HCV RNA with Amplicor 2.0. Cases were systematically tested for HIV antibodies. Chi-square test and unconditional logistic regression were used to estimate the odds ratio (OR) and 95 percent confidence interval (95% CI) for lymphoma associated with HCV. All statistical tests were two-sided.
Results: HCV infection was detected in 40 cases (7.5%) and 23 (3.8%) control subjects. HCV in sera was present in six of 16 patients with HIV-related lymphomas and in four of eight organ-recipient-related lymphomas. HCV was associated with a two-fold increased risk for lymphoma [odds ratio (OR)= 2.06 95%CI= 1.21-3.50] as compared to HCV negative subjects, with nearly identical results [OR=2.04 (95%CI=1.42-3.66)] with HCV status defined by HCV viremia. Among non-HIV subjects the OR for all lymphomas was 1.82 (95%CI =1.05-3.17) and among non-organ recipients the OR was 1.85 (95%CI=1.08-3.18). Among all lymphoma categories, HCV was most strongly associated with diffuse large-cell lymphoma (OR=4.08, 95%CI=1.91-8.71). This risk was reduced when HIV or organ allograft transplant status was controlled for (OR=2.20 95%CI= 0.84-5.73). Among non-immunocompromised subjects, a two-fold increased risk associated with HCV was also observed for marginal B-cell lymphomas and Hodgkin's lymphomas, but the associations were not statistically significant.
Conclusions: HCV infection is associated with an increased risk of lymphoma, although the mechanism of this association has not been well defined.

046

ASSOCIATION OF TUMOURS OF THE GALLBLADDER AND THE BILIARY TRACT WITH MEDICAL CONDITIONS AND LIFESTYLE IN MEN - FIRST RESULTS OF O EUROPEAN MULTI-CENTRIC CASE-CONTROL STUDY

Wolfgang Ahrens[1], Antje Timmer[2], Mogens Vyberg[3], Jørn Olsen[4]. En nombre del Grupo: Rare Cancers Study Group

[1]Bremen Institute for Prevention Research & Social Medicine, University Bremen, Bremen, Germany. [2]University Clinics, Regensburg, Germany. [3]Institute of Pathology, Aalborg Hospital, Aalborg, Denmark. [4]Department of Epidemiology and Social Medicine, Aarhus University, Aarhus, Denmark.

Introduction: This study was designed to identify yet unknown and possibly rare causes of cancer of the gallbladder and the extrahepatic biliary tract that could be amenable to preventive measures.
Methods: Newly diagnosed male cases in the age-group 35 to 70 years were recruited between 1995 and 1997 in a population-based multi-centric case-control study involving six European countries (Denmark, Sweden, France, Germany, Italy, and Spain),. A central reference pathologist confirmed a tumour of the extrahepatic bile ducts (EBD), the gallbladder (GB), or of the Papilla Vateri (PV) included in the analysis. Randomly selected controls from the general population were frequency-matched by age and study region to the cases. Hospital controls were drawn in two study centres. All participants were interviewed in person using a standardised questionnaire. If a case was too ill or had died a surrogate person was interviewed. Medical conditions were assessed as being confirmed by a physician and being present at least three years prior to diagnosis and interview. The statistical analysis was performed by chi-square-tests and logistic regression using the SAS programme package. Odds Ratios (OR) were adjusted for age (5-year age groups) and region of residence.
Results: 253 cases (83 EBD, 79 GB, 80 PV, 11 overlapping) fulfilled the inclusion criteria (97% adeno-carcinoma). There was no age difference between these localisations. The analysis included 186 cases and 1969 controls for whom interviews were available. The interview-response was 74% and 66% for cases and controls respectively. Gallstones were confirmed as a risk factor for GB (OR 2.2; 95% confidence interval [CI] 0.91-5.36), EBD (OR 2.6; 95% CI 1.06-6.32) and PV (OR 1.5; 95% CI 0.52-4.25). Cholecystectomy (CCE) was associated with all biliary tumours combined (OR 1.5; 95% CI 0.51-4.39). Due to the low prevalence of CCE (5%) we were unable to investigate differences by localisation. Diabetes was associated with GB (OR 2,6; 95% CI 1.12-5.95). For a body-mass-index [BMI] >30 at the age of 35 an excess risk was observed relative to a normal BMI (BMI 18.5-25) (OR 1.74; 95% CI 0.88-3.43). This relationship was more pronounced for the BMI based on the smallest weight during adult life, while this was not the case for a BMI >30 one to five years prior to diagnosis (OR 0.96; 95% CI 0.56-1.64). There was no convincing evidence for an association between biliary cancer and a history of diabetes mellitus, hepatitis or typhus abdominalis. Also smoking, alcohol consumption, and education showed no association with this cancer.
Conclusions: Gallstones were confirmed as the most important risk factor for biliary cancer. Apart from overweight we did not find any factors related to lifestyle that were associated with this cancer.

047

EUROCHIP: AN EUROPEAN PROJECT FOR THE CANCER SURVEILLANCE. THE ROLE OF SPAIN

Andrea Micheli[1], Carmen Navarro[2], Paolo Baili[1], Marina Pollan[3], Isabel Izarzugaza[4], Isabel Garau[5], Nieves Ascunce Elizaga[6], Carmen Martinez[7]. Eurochip: An European Project for the Cancer Surveillance

[1]Unit of Epidemiology, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy. [2]Consejería de Sanidad Murcia, Spain. [3]National Center for Epidemiology Carlos III, Madrid Spain. [4]Basque Country Cancer Registry, Spain. [5]Mallorca Cancer Registry, Spain. [6]European Breast Cancer Network, Spain. [7]Granada Cancer Registry, Spain.

Introduction/background: Despite the concern on cancer, a monitoring system covering all European Union (EU) countries did not yet exist. EUROCHIP (European Cancer Health Indicator Project) thus aimed to produce a comprehensive list of cancer health indicators pertaining to cancer, with variables describing the natural history of the disease: occurrence, clinical follow-up, recurrences, patient survival, diagnostic and therapeutic procedures, effectiveness of care, outcome and care prevalence. The project was conceived as part of a large-scale Health Monitoring Programme (HMP), supported by the European Commission, that has been implemented to set EU health indicators. It was mainly intended as an intellectual work organised to reach the maximum consensus on a list of indicators. EUROCHIP chose variables according to criteria of easy collection, comparability and grade of each country's representation and hence proposed standardised methods for collection. Final aim of the project is to improve cancer surveillance and promote actions in all European countries to reduce inequalities in controlling tumours.
Methods: A complex organisation was set up. Each indicator was discussed in several meetings at both national and international levels. International meetings on different domains (prevention, epidemiology and cancer registration, screening, treatment and clinical aspects, and social and macro-economic variables) was organised. We aimed to achieve a general consensus for several aspects of the indicators: i.e. description, operational definition, meaning, possible use, caveat, modalities of classification, possible sources, standardisation and validity. The final list was obtained from discussions on priorities which, as a whole, added value to the indicator, highlighted problems on comparability among European countries, on data collection and on the relative costs.
Results: More than 130 cancer specialists of 15 countries belonging to different fields were involved in the various phases of the project. EUROCHIP produced a list of indicators collectable in the next years in each European country for the development of a large European health database. A European set of data is presently being constructed.
Conclusions: This presentation aims to present the results EUROCHIP to the Spanish epidemiological audience. The meaning of the indicators will be given. However, a new phase is now in progress. It is our intention to organise a group of cancer specialists in different countries to discuss the available data to monitor cancer control. The goal will be to reduce disparities, fight inequalities and increase the capability of the national health system in cancer surveillance.

048

SERUM CONCENTRATIONS OF HIGHLY PREVALENT ORGANOCHLORINE COMPOUNDS AND RISK OF EXOCRINE PANCREATIC CANCER: A CASE-CONTROL ANALYSIS

Miquel Porta[1], Ekhine Zumeta[1], Laura Ruiz[1], Manuel Jariod[1], Núria Malats[2], Joan Alguacil[3], Alfredo Carrato[4], Francisco X. Real[5], Joan O. Grimalt[6]. En nombre del Grupo: PANKRAS II Study Group

[1]GRECMC, IMIM, Barcelona, Spain. [2]URRA, IMIM, Barcelona, Spain. [3]Occupational & Environmental Epidemiology Branch, NCI, Bethesda, USA. [4]Hospital General d'Elx, Universitat Miguel Hernández, Alacant, Spain. [5]URBCM, IMIM, Barcelona, Spain. [6]Environmental Chemistry, CSIC, Barcelona, Spain.

Introduction: Whilst knowledge on the etiology of exocrine pancreatic cancer (EPC) is limited, organochlorine compounds (OCs) as DDT, DDE and polychlorinated biphenyls (PCBs) may increase the risk [1,2], and several mechanistic scenarios have been proposed [1-3].
Methods: All EPC cases newly diagnosed at 5 general hospitals were prospectively included (n=185). Over 88% were personally interviewed in-hospital. Serum concentrations of OCs were measured by high-resolution gas chromatography with electron-capture detection in 144 patients, thus increasing by 182% the sample size of our previous, early report [1]. Cases were compared with 27 conventional hospital controls recruited in one of the study hospitals among subjects admitted for benign, non-digestive disorders. Multivariate-adjusted odds ratios (OR) and their 95% confidence limits (CL) were computed by unconditional logistic regression.
Results: Serum levels of p,p'-DDT and p,p'-DDE were significantly higher in cases than in controls: the respective medians (mcg/g lipid) were, for DDT, 0.42 and 0.20 (p = 0.04), and for DDE, 2.70 and 1.26 (p <0.01). The OR for the upper (>0.574 mcg/g) vs. lower (<0.205 mcg/g) tertile of p,p'-DDT, adjusted by age, sex, tobacco, alcohol and coffee consumption (ORa) was 4.52 (CL: 1.36 and 14.97; p for trend = 0.012). The ORa was similar for p,p'-DDE (p-trend = 0.006). These estimates held when adjusting by other OCs; e.g., the ORa for the mid (1.441-3.970 mcg/g) vs. lower (<1.441) tertile of p,p'-DDE, further adjusted by PCBs 138, 153 and 180, hexachlorobenzene (HCB) and â-hexachlorocyclohexane (â-HCH) was 5.22 (CL: 1.37 and 19.96); the corresponding figure for the upper tertile (>3.970) was 7.57 (CL: 1.53 and 37.40) (p for trend = 0.009). Most ORa for PCBs, HCB and â-HCH were in the range 1.49 to 1.87, and none was statistically significant. Thus, the association between levels of OCs and risk of EPC was not indiscriminate with all OCs: concentrations of HCB and â-HCH in cases were high (median of 1.46 and 0.86 mcg/g, respectively), and yet these two compounds were not associated with an increased risk. Concentrations of DDE were twice as high in our cases than in cases from San Francisco, USA [2], while those of HCB were over 66 times higher in our study. Concentrations of PCBs are hard to compare because different congeners were analysed in each study [1,2].
Conclusion: Organochlorine compounds as p,p'-DDT and p,p'-DDE may increase the risk of exocrine pancreatic cancer. The results truly need to be refuted or replicated by new studies, which should also assess interactions among OCs, and of OCs with other environmental exposures and with genetic factors.

References:
1. Porta M et al. Lancet 1999.
2. Hoppin JA et al. Cancer Epidemiol Biomarkers Prev 2000.
3. Porta M et al. Molec Carcinogenesis 2003.