1042 POSTER

Peritoneal carcinomatosis from colorectal origin: correlation of preoperative CT with intraoperative findings and evaluation of interobserver agreement

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Background: In patients with colorectal cancer, it is important to diagnose peritoneal carcinomatosis as well as to detect location and size of peritoneal tumor dissemination in view of treatment planning. The aim of this study was to investigate the correlation of preoperative CT with intraoperative findings as well as interobserver differences in such patients.

Materials and methods: Preoperative CT-scans from 25 consecutive patients with peritoneal carcinomatosis from colorectal origin were independently reviewed by two radiologists and their observations were compared with operative findings. The presence of tumor deposits and the diameter of the largest tumor deposit were noted in seven abdominopelvic areas.

Results: The presence of peritoneal carcinomatosis was detected in 60.0% and 76.0% of those patients by each radiologist separately (p=.36). The detection rates of peritoneal implants in the defined abdominopelvic areas per tumor size for each radiologist were 9.1% and 24.3% for tumor size < 1 cm, 14.3% and 28.2% for tumor size 1-5 cm, and 59.3% and 66.7% for tumor size > 5cm. Regarding tumor size, a poor correlation was observed between peroperative and CT scores (κ =0.11–0.23), while agreement between both radiologists was moderate (κ = 0.484). Overall sensitivity, specificity and accuracy for tumor involvement per area were 24.5%, 94.5% and 53.0% respectively for one radiologist, and 37.3%, 90.4% and 60.0% respectively for the second radiologist. Accuracy of tumor detection varied widely per anatomic site and was poorest for the ileocaecal area, the omentum and transverse colon, and the mesenterium and small bowel. Statistically significant interobserver difference was noted, specifically for tumor size of 1-5 cm and localization on omentum and transverse colon. Fictive paired CT-reading improved significantly results of one of the radiologists.

Conclusions: The presence of peritoneal carcinomatosis was moderately diagnosed by the CT-readers. Accuracy of detection of individual peritoneal metastases from colorectal origin was poor, especially for small tumor deposits and at certain abdominopelvic areas. Statistically significant interobserver differences were noted. Paired-observer CT interpretation may potentially improve results of a single radiologist.

Public health and cost

1043 POSTER

Reassessment of GSTM1 and GSTT1 cancer predisposing roles: comparison of genotypes in elderly tumor-free smokers and non-smokers vs. healthy donors vs. lung cancer patients

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Background: Studies on low-penetrance cancer-predisposing polymorphic genes suffer from poor reproducibility, that justifies a need for novel, more efficient approaches.

Material and methods: To reassess the controversial evidence for the role of GSTM1 and GSTT1 deficiencies in cancer susceptibility, we included in the molecular epidemiological study an additional, highly demonstrative cohort, namely elderly tumor-free subjects (elderly donors, ED). ED, especially smokers, are likely to accumulate cancer-resistant genetic variants, thus, if a particular at-risk genotype indeed plays a role in tumor susceptibility, it should be under-represented in this group.

Results: Comparison of ED smokers and non-smokers vs. healthy donors (HD) vs. lung cancer patients (LC) confirmed a modest unfavorable impact of GSTM1 but not GSTT1 null genotypes. In particular, GSTM1(-) variants were underrepresented in ED vs. HD (146/324 (45%) vs. 184/339 (54%); OR = 0.69 (0.51 - 0.94), P = 0.018). The prevalence of GSTM1 deficiency in LC (91/167 (54%) did not statistically differ from the one observed in HD, however showed a significant increase when ED served as a non-affected control (OR = 1.46 (1.00 2.12); P = 0.048). Furthermore, in agreement with mechanistic considerations, an excess of GSTM1(-) genotypes was more pronounced in squamous cell carcinoma (SCC) cases (51/88 (58%)) as well as in LC patients with seemingly low cumulative carcinogen exposure dose (non-smokers: 12/19 (63%); patients aged below 50 years: 13/17 (76%)). Contrary to GSTM1, GSTT1 polymorphism did not display regular deviations between the studied groups.

Conclusions: The results of this study are in good agreement with the body of literature data, including several published meta-analyses. The suggested study design involving additional cancer-resistant group of non-affected subjects may provide highly demonstrative data and seems to be suitable for pilot investigations as well as resolving of controversial issues.

1044 POSTER

High incidence of mutations in BRCA1 in breast and ovarian cancer patients in Latvia

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Background: Apart from educating the community, implementation of screening tests, the incidence of breast cancer in western countries is continuously growing. Early detection of suspect breast cancer is crucial to successful treatment. An estimation of risk groups should be involved here. As one of these groups could be women having a genetic determinant for breast or ovarian cancer.

Morbidity rate from breast cancer in Latvia is taking a stable first place among other cancer diseases. On its turn, the death rate from ovarian cancer in Latvian women takes the high third place.

Few cases - up to 15 per cent - of all breast and ovarian cancers are inherited through autosomal dominant. In most cases, it appears to be linked to familial breast and ovarian cancer syndrome caused by mutations in the BRCA1 gene.

Hereditary breast/ovarian cancer features chance of developing the disease at an early age and a high risk of developing it in the other breast.

The objective of our study was:

- to identify the spectrum of mutations in the BRCA1 gene in Latvian breast and ovarian cancer patients;
- to assess the possibilities of identifying high-risk individuals in Latvia;
- to find out criteria to be followed referring patients for genetic testing;
- to develop a strategy of preventive measures and treatment offered to high-risk women.

Material and methods: During the first stage of our study (1996-2001), the spectrum of mutations in the BRCA1 gene in Latvian breast and ovarian cancer patients was identified. The analysis was carried out in several patient groups: with or without a family-history of breast and/or ovarian cancer; of different age groups; in cases of sporadic cancer not having a positive familial anamnesis.

The results of precedent study proved that 90 per cent of individuals carrying mutations develop cancer before aged 48. Therefore, patients of two age groups - under and over 48 - having differing familial anamnesis of cancer underwent genetic testing during last couple of years.

BRCA1 gene was screened for mutations in all coding sequence and 5′- and 3′- flanking intronic sequence of each exon by SSCP/HD analysis and direct sequencing of variants detected.

Results: The analysis of the mutations' spectrum determined that three prevalent mutations account for about 90 per cent of all mutations in the BRCA1 gene, one of them (5382insC) - in about 60 per cent of cases. An average age at which female carrying mutations develop breast cancer is under 38.

Referring 94 patients suffering from breast cancer to full BRCA1 testing showed totally 23 mutations.

Interesting:

Under 48	58 patients	21 mutations	36.2%
Over 48	36 patients	2 mutations	5.6%

142 women having breast cancer were referred to the BRCA1 screening tests on three prevalent mutations. As a result, 42 mutations were detected.

In cases of ovarian cancer, 30 patients underwent a full and another 30 - a partial BRCA1 gene testing (on three prevalent mutations). Consequently, 19 mutations were detected.

Currently, 84 mutations of the BRCA1 gene are detected in Latvia, of which 60 are deleterious.

Conclusion:

- Testing of three BRCA1 gene mutations in all breast-cancer patients of reproductive age in Latvia could provide an opportunity to identify more than 100 high-risk families a year.
- Incidence of breast and ovarian cancer at an early age is an indicative of a possible link to a hereditary mutation.
- Founder effect detected in Latvia will make genetic testing mere cost-effective.

1045 POSTER

Rare tumour survival in adult European patients

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Background: Most rare tumours present major clinical problems. Their rarity renders in depth study of natural history and identification of optimum treatment guidelines problematic, and early and accurate diagnosis sometimes difficult. Publications on these tumours typically derive from centres of excellence, which do not reflect the situation at the population level. The EUROCARE database presents a unique opportunity to investigate rare cancers in Europe at the population level. The aim of this communication is to describe survival of adult European patients with some rare tumours according to major demographic and clinical variables. Survival time trends and, depending of the number of cases, survival variations in different regions and countries will also be presented.

Material and methods: The European survival figures for the period of diagnosis 1983-94 were derived from the EUROCARE database. The data were contributed by about 65 registries in 21 countries. The rare tumour chosen was on the basis the criteria reported above: very low incidence, treatment problems, follow-up difficulties, geographic variation, lack of literature. The rare cancer sites selected were: angiosarcoma of liver, mesothelioma, adenocarcinoma of cervix, sarcoma of uterus, anal squamous carcinoma, testis cancer in old men, soft tissue sarcoma of limb.

Results: Five-year relative survival for these rare cancers diagnosed between 1983-94 will be analysed and will be described by sex, age, period of diagnosis and large regions. When available stage and therapy will be introduced in the analysis.

Conclusions: The EUROCARE project provides a unique opportunity to study uncommon cancer survival at the population level. Topography with morphological codes will be considered in order to identify rare diagnostic categories of interest. For most rare cancers in the EUROCARE database, the proportion of microscopically confirmed cases is high, indicating good quality data and also the existence of detailed information on morphology.

1046 POSTER

A definition of what a rare tumor is.

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Background. Medical decisions, clinical research, and healthcare organization pose unique difficulties in rare tumors. In fact, clinical decisions are to be based on weaker evidence; clinical trials are less easy to perform and the development of new drugs (orphan drugs) should receive incentives; patient referral could follow different criteria from frequent tumors. However, a specific definition of rare tumors is lacking. On the other hand, definitions of rare diseases do exist, and they are based on prevalence. In Europe, rare diseases are defined as those with a prevalence <50/100,000.

Material and methods. The EUROCARE database was used in order to provide estimates of the incidence of rare tumors in Europe. The ITAPREVAL database was used in order to provide estimates of the prevalence of rare tumors in a European country such as Italy. Results were compared and evaluated by a group of clinicians and epidemiologists.

Results. If the European definition of rare diseases were used also for tumors, by using the sole ICDO codes for tumor topography, a proportion in excess of 10% of tumor sites would be placed among rare diseases. They would include also esophageal cancer, brain tumors, pancreatic tumors, and leukemias, which have an incidence >3/100,000/year. On the other hand, tumors such as testicular cancer and thyroid gland tumors, with an incidence <3/100,000/year, would not be considered rare, their prevalence being not so lower than that of one of the most frequent tumors, lung cancer.

Conclusions. Prevalence is a good criterion to define mainly chronic, slowly or non-evolving, rare diseases. In cancer, however, clinical, research, and organizational problems are often stage-specific and related to some windows in the natural history of the disease. Patients with some cancers may be often cured soon after diagnosis, while those with other cancers may not be, and require continuous care. Therefore, the diverse prognosis of different tumors gives rise to inconsistencies if prevalence is used to split them into rare and frequent. In conclusion, a list of rare tumors is under development, based on ICDO codes for topography, morphology, and a combination of both, by using incidence, not prevalence, as a criterion. An incidence threshold around 3/100,000/year might well define a group of tumors likely to be felt as rare by clinicians. A consensus development process about that should then be promoted within the oncology community.

1047 POSTER

Cohort analysis of prostate cancer mortality in the male population of Belgrade

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Background: The objective of this analysis was to estimate prostate cancer mortality rates and their trends in the male population of Belgrade, during the period 1975-2001, with special emphasis on the assessment of age-period-cohort effects.

Method: The source of mortality data were official death certificates for Belgrade population for mentioned period of time. For calculation of mortality rates, the population denominator data were obtained from the 1981 and 1991 national census data with interpolation. The total population of Belgrade was about 1.6 million during the period observed (1975–2001). Age standardization was done by the direct method using world population as a standard. Regression coefficient was determined by Fisher's test.

Results: In Belgrade, prostate cancer is the 4th most common cause of cancer death in males, representing 6.52% of male cancer deaths. Average annual standardized mortality rate was 10.13 per 100,000 male population (95%CI-confidence interval 9.00-11.26). Mortality rate showed significantly increasing tendency for observed period-y=6.603+0.259x, p=0.001. In the age group up to 50 average age-specific mortality rate was 0.16/100,000 (95%CI 0.01-0.89). The highest age-specific mortality rate was registered in the age group over 75 years with average value of 229.49/100,000 (95%CI 199.30-259.68). Significantly increasing trends for age-specific mortality rates were registered in all age groups above 60, however the highest increase was in the age group 70-75 (y=173.269+4.136x, p=0.001). In cohort analysis of age-specific death rates, all age groups of the youngest birth cohorts (1925-1929) have 3-4 times higher prostate cancer mortality risk than birth cohorts of the oldest generations (1900-1904).

Conclusion: According to obtained findings, increasing tendency for prostate cancer mortality in Belgrade, especially in younger generations, should be expected to continue in the future.

1048 POSTER

Estimate of the pulmonary neoplastic hazard of inhaled depleted uranium in gulf war veterans

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The aim of this study was to evaluate the concentration of inhaled aerosols of depleted uranium oxide in the lungs of Allied Forces Gulf War Veterans during operation Desert Storm. Five British, Canadian, and US veterans were analyzed for the quantitative relationship of four uranium isotopes in the urine, by thermal ionization mass spectrometry. The biological half-life of DU was derived form the Batelle interstitial lung fluid model and the pulmonary DU burden was calculated for time-zero. The total number of alpha radiation events was determined by integrating the value of a 24-hour urinary excretion of depleted uranium from time-zero to the actual measurement time, ten years after exposure. Average 24-hour urinary specimens of five subjects contain 3.27×10^{-2} μg of DU corresponding a time-zero inhalation of 0.336 mg of DU with a resulting dose of 0.958 mSv in the first year and 4.86 mSv within ten years. Our values of the upper limit of maximum permissible inhalation dose of total uranium provide a model for the assessment of neoplastic risk of inhaled depleted uranium and warrants further research with a particular reference to pulmonary neoplastic risk of inhaled aerosols of ceramic oxides of depleted uranium.