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

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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.