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Chemotherapy-Related Thrombocytosis and Its Association With Thromboembolism (TE)

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Background: Chemotherapy such as antimetabolites increases the risk of thrombo-embolism (TE) in patients with cancer. Although thrombocytopenia is a known side effect of chemotherapy, antimetabolites-related thrombocytosis is uncommonly reported. The study aimed to determine the incidence of gemcitabine-related thrombocytosis and its risk associated with TE.
Methods: Medical records of 250 consecutive adult patients with a malignant disease who received gemcitabine alone or in combination with a platinum compound at the Saskatoon Cancer Center were reviewed. Patients with history of prior TE or with baseline thrombocytosis were excluded. A multivariate analysis was done to determine factors associated with TE.
Results: 220 eligible patients with median age of 63 yrs (range: 26−83) and M:F of 1:1 were identified. 209 (95%) patients had advanced malignancy; 92 (42%) had lung cancer and 130 (59%) had received prior chemotherapy. 151 (69%) patients received gemcitabine in combination with a platinum compound. Median number of cycles were 4 (1−8). 45 (20%) patients had white blood cell (WBC) count of $>11\times10^9$/L. Median platelets count prior to commencement of gemcitabine was 300×10^9/L (range: 44–449). 102 (46%) patients experienced thrombocytosis within 4 weeks of chemotherapy. Median post-gemcitabine platelet count in patients with thrombocytosis was 632×10^9/L (range: 457–1385). Median duration of thrombocytosis was 2 weeks (range: 0.5−10). 21 (10%) of 220 patients experienced a vascular event (venous, n = 14; arterial, n = 7) within 6 weeks of treatment. Median platelet count prior to a vascular event was 297×10^9/L (79–669). 9 of 102 (9%) patients with thrombocytosis experienced a vascular event compared with 12 of 118 (10%) patients without thrombocytosis (p=NS). On multivariate analysis luekocytosis (odd ratio [OR] 5.8 [95% CI: 2.1–15.8]) & comorbid illnesses (OR 4.1 [95% CI: 1.4–12.6]) were correlated with TE.
Conclusions: Although gemcitabine has been associated with an increased incidence of thrombocytosis, chemotherapy-related thrombocytosis does not increase the risk of TE in cancer patients. Of note elevated white blodd cells count and underlying comrobid illnesses increase the risk of TE in such patients.

3526 POSTER

Social Determinants and Survival of Thyroid Cancer in Iran, 2001–2005

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Background: Thyroid cancer is the most common malignancy of endocrine system in the world. It is the 7th most common cancer in females, 14th in the males and the 11th most frequent cancer in both sexes in Iranian population. The present study aimed to determine survival of thyroid cancers in Iran based on sex, age group, pathology and geographical variation.
Methods: The patients selected for this study were 602 out of 5759 cases which were listed by cancer registry system between 2001 and 2005. Kaplan–Meier method was used for survival estimation and Cox's proportional hazard model used for calculating hazard ratio according to demographic and risk variables.
Results: The overall 5-year survival rate was 88.0%. There was significant difference between the survival of two sexes. The best and worse survival were in the age group under 40 and over 60 years old, respectively. The best survival was in papillary type, and anaplastic type belongs to worst survival. The best survival was in southwest (Khuzestan) area and the worse was estimated in northwest (Azarbaijan).
Conclusion: Size of young population and social determinants would be important effective elements for different survivals. These determinants should be in more consideration in managing chronic disease such as thyroid cancer.

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Correlation of GSTP1, GSTM1 and CYP1A1 Gene Polymorphisms and Lung Cancer Risk Among Smokers in a Greek Population

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Background: Lung cancer is the leading cause of cancer mortality worldwide and tobacco smoking has been established as its most important risk factor. Cigarette smoke contains several chemical compounds which are known carcinogens. Most of them need to be activated by phase I enzymes, such as cytochrome P450 (CYP), while phase II enzymes, such as glutathione S-transferases are responsible for the detoxification of activated forms. The present study intended to determine the role of CYP1A1, GSTP1 and GSTM1 gene polymorphisms in smoking-related lung cancer risk among Greeks.
Methods: One-hundred non-small and small cell lung cancer patients and 100 healthy controls with smoking history participated in the study. Basic demographic characteristics were well-balanced between the two groups. The participants were screened for the presence of the following polymorphisms: MspI (CYP1A1), Ile105Val (GSTP1) and GSTM1-null. Lung cancer risk was estimated as odds ratio (OR) and 95% confidence intervals (CI) using regression analysis.
Results: There was a statistically significant difference in genotypes GSTP1 Ile/Val (p = 0.004) and GSTM1-null (p = 0.011) between the two groups. Conversely, there was no difference in the presence of MspI polymorphism among the participants. Also, GSTP1 Ile/Val and GSTM1-null genotypes were associated with increased lung cancer risk. Furthermore, the combination of wild-type genotypes was shown to be correlated with reduced lung cancer risk by 69% (95% CI= 38−84%, p = 0.001).
Conclusions: The results of the study suggest that GSTP1 and GSTM1 gene polymorphisms contribute to increased lung cancer susceptibility in Greek smokers and that the combination of wild-type genotypes significantly reduces lung cancer risk.

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Prevalence of BRCA1 and BRCA2 Germline Mutations Among Pakistani Patients With Triple Negative Breast Cancer

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Background: Current criteria for *BRCA1/2* genetic testing rely primarily on family history of breast/ovarian cancer and early age of onset. In this study we assessed if the triple-negative breast cancer phenotype (negative for estrogen receptor, ER; progesterone receptor, PR and human epidermal growth factor receptor 2, HER2) can be used to identify candidates for *BRCA1/2* mutation testing in Pakistan.
Materials and Methods: Three hundred and sixty-seven unrelated women diagnosed with breast cancer below or equal 30 years of age (n = 169) or a family history of breast/ovarian cancer (n = 198) were ascertained at the SKMCH & RC from June 2001 to September 2010. Clinical and histopathological data and blood samples for DNA isolation were obtained from all patients. Comprehensive *BRCA1/2* mutation screening was performed using protein-truncation test, single-strand conformational polymorphism analysis, and denaturing high-performance liquid chromatography analysis followed by DNA sequencing of variants detected in these assays.
Results: On the basis of clinical ER, PR, and HER2 testing 141 (38.4%) out of 367 women presented with triple-negative breast cancer. Forty-eight of them (34%) carried a deleterious mutation, 45 in *BRCA1* and three in *BRCA2*. In the group of patients with early-onset triple-negative breast cancer 9/66 (13.6%) carried a *BRCA1* mutation. Among the familial breast/ovarian cancer patients 39/75 (52%) carried a mutation, 36 in *BRCA1* and three in *BRCA2.* Triple-negative breast cancer in *BRCA1/2* carriers and non-carriers were diagnosed at different median ages of diagnosis, 30 years (range 22−54) and 28 years (range 19−67),

respectively; $p = 0.04$, Exact Wilcoxon rank-sum test). There were no differences in histological type, tumour size, grade and lymph node status between the groups.
Conclusions: Our data show that Pakistani women with early-onset triple negative breast cancer are candidates for genetic *BRCA1* testing, even in the absence of a family history of breast/ovarian cancer.

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Effect of Sample Type and Turnaround Time (TAT) on the Feasibility of Non-Small Cell Lung Cancer (NSCLC) Epidermal Growth Factor Receptor (EGFR) Mutation Testing in Routine Clinical Practice: Results From the Spanish REASON Study

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Background: The presence of EGFR mutations guides treatment selection in NSCLC. Albeit Biopsy samples (s) are a gold standard for mutational analysis, they are difficult to obtain in many cases, and mutational analysis must be performed on cytologies (cyt) s instead. One of the purposes of the Spanish REASON epidemiological study was to gain insight into variables that affect the feasibility and implementation of EGFR mutation testing (tissue vs cyt and TAT) in routine clinical practice.
Material and Methods: All newly diagnosed advanced NSCLC patients in 39 Spanish centres nationwide were included prospectively for a 6-month period. Mutation testing was performed mainly through a centralized diagnostic platform that employed two central laboratories (787 s), or on-site (222 s) where EGFR mutation testing was customary (7 laboratories). Methodologies used for EGFR mutation testing were Qiagen's Therascreen EGFR PCR Kit™ (452 s), direct sequencing (89 s), fluorescent PCR fragment analysis for exon 19 deletions (del) (480 s), and allelic discrimination using fluorescence probes (450 s) or PCR enzymatic restriction (26 s) for exon 21 L858R mutation.
Results: 1009 p with available s were included in the analysis (800 tissue and 209 cyt). 15.2% of s were from non-smoking patients. 23.9% of tissue s were of squamous histology vs 16.3% of cyt. 68 s (6.7%) were inadequate for mutation analysis (6.1% tissue, 9.1% cyt). Median overall TAT was 9.7 days (9.7 days tissue, 9.5 days cyt). Median TAT for a centralized diagnostic platform was almost 7 days lower than on-site testing (8.5 days vs. 15.3 days). 941s were screened for major mutations, 504 of which were additionally analyzed for the presence of minor mutations. Mutation rates according to s type and exons analyzed are presented in Table 1.

Table 1

	Mutation rates, n (%)		
	Tissue	Cyt	Total
Major mutation rates	**N = 751**	**N = 190**	**N = 941**
Del 19 or L858R	89 (11.9)	19 (10)	108 (11.5)
Del 19	72 (80.9)	17 (89.5)	89 (82.4)
Exon 21 L858R	17 (19.1)	2 (10.5)	19 (17.6)
Minor mutation rates	**N = 394**	**N = 110**	**N = 504**
Minor mutations	15 (3.8)	7 (6.4)	22 (4.4)
Exon 18	5 (33.3)	3 (42.9)	8 (36.4)
Exon 20	6 (40)	1 (14.3)	7 (31.8)
Exon 21 (except L858R)	4 (26.7)	3 (42.9)	7 (31.8)

Conclusions: Given the similar adequacy for molecular analysis and mutation rates observed in cytological vs. tissue s, cyt seem to be amenable to mutation analysis. Moreover, mutation testing through a diagnostic platform warrants a centralized diagnostics model for implementation in routine clinical practice.

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The Impact of Early Thromboembolic Event on Overall Survival in Cancer Patients

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Background: Thromboembolic events (TE) are common complication of cancer, may lead to mortality and detoriate quality of life. "Initial period", (first 3 months) after the diagnosis of cancer holds the highest risk for development of cancer-associated TE.
Material and Method: Between October 2007 to March 2011, we retrospectively evaluated the occurence of TE in patients with histologically confirmed solid tumours. The diagnosis of TE is confirmed by radiology and patients were treated accordingly. One hundred seven of 1838 patients (5.8%) were diagnosed as TE. Twenty nine of 107 patients (%27) had TE at initial period and 78 (%73) had TE at delayed (later than three months) period.
Results: There was no statistical significant relationship for age and gender between TE and non-TE groups. Forty three (41%) had distal lower extremity (DLE)deep venous thrombosis (DVT), 33 (31%) had PE and the rest includes 15 central/proximal DVT (14%), 8 PE with DLE DVT (7%), 6 central venous catheter-related DVT (5%) and 2 upper extremity DVT(2%). Frequencies for TE according to histopathology were; Non Hodgkin's lymphoma (6/36 = 16.7%), pancreatic cancer (13/79 = 16.5%), gastric cancer (18 /152 =11.8%), NSCL (adenocarcinoma) (9/82 = 11%), GBM (4/53 = 7.5%) and colorectal cancer (22/312 = 7%). Median survival was 30.5 months for TE group and 127 months for non-TE group (log-rank, p = 0.0001). Median time from diagnosis to TE was 7.25 months. Median overall survival was 15 months and 34.25 months for patients with TE at initial period and with delayed TE (log-rank, p = 0.011), respectively. The diagnosis of TE were more frequent in advanced stage (stage I-II vs stage III-IV, 13/107 = 12% vs 94/107 = 88% respectively, p = 0.0001) and with histology of adenocarcinoma (86/107 = 80% vs 21/107 = 20% respectively, p = 0.01). Odds ratio (OR) for TE in patients with adenocarcinoma histology was 1.9 [95% confidence interval (CI):1.2−3], and with advanced stage, OR was 4.35[95% CI:2.42–7.84]. OR for TE in patients with adenocarcinoma at advanced stage was 2.54[95% CI:1.44–4.49].
Conclusions: In our patient cohort, having TE at initial period, histology of adenocarcinoma and advanced stage emerged as independent prognostic factors for poor survival in cancer patients.

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Urinary Bladder Cancer and Potential Risk Factors in Lebanon − a Case-control Study

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Background: Given the strikingly high bladder cancer incidence in Lebanon, estimated to be the second most common malignancy among Lebanese men, coupled with the potential effect of Phase I and Phase II drug-metabolizing enzymes on bladder cancer risk, a case control study was conducted in Lebanon to investigate the potential risk factors for bladder cancer.
Study design:159 male cases and controls (54 cases and 105 controls) were selected from two tertiary care centers in Lebanon: St. George Hospital and Bahman Hospital. Cases were men, 50 years and older, with primary confirmed bladder carcinoma. They were randomly selected as per year of reporting. Controls were hospital based, 50 years and older, with no present or previous history of cancer or any systemic illnesses. Informed consent was obtained on all cases and controls and the study gained IRB approval from the respective hospitals. Data were collected using a structured face to face interview questionnaire gathering information on history of known urinary bladder cancer risk factors such as age, family history, smoking habits, drinking, dietary habits, chronic diseases and urinary infections, use of hair dyes, and occupation. Laboratory blood testing was performed to determine N- Acetyltransferase1 (NAT1) genotype. Univariate, bivariate and multivariate logistic regression analyses were used to analyze the data, check for effect modification and control for confounders.
Study results: Results highlighted the importance of smoking, occupational exposure to fumes and vapors, prostate related diseases, as well as NAT1*14A allele as independently significant risk factors for bladder cancer. The odds of having bladder cancer among smokers was 1.02 times higher in cases than controls. The odds of occupational fumes/vapors exposure was 4.34 times higher in cases than controls. The odds of prostate related diseases was 7.8 times higher in cases than controls.