Do Polygenic Risk Scores For Cancer Susceptibility Associate With Risk Of Radiotherapy Toxicity?


Materials/Methods: All patients (n=512) who underwent radiotherapy between 2002-2004 and who were included in the breast (n=108), prostate (n=475), or lung (n=295) cancer cohort of the REQUITE consortium were analyzed for polygenic risk scores (PRS). This score is calculated using genome-wide association study (GWAS) results and measures lifetime risk of developing cancer. Multivariable logistic regression tested association between PRS and toxicity, with the addition of a shared risk.

Results:PRS associated with increased risk of developing cancer for breast (odds ratio: 1.10, 95% confidence interval: 1.00 to 1.03), prostate (odds ratio: 1.12, 95% confidence interval: 1.00 to 1.03), and lung cancer (odds ratio: 1.12, 95% confidence interval: 1.00 to 1.03). However, no association was found between PRS and development of late radiotherapy toxicity among breast (odds ratio: 1.01, 95% confidence interval: 1.00 to 1.02), prostate (odds ratio: 1.01, 95% confidence interval: 1.00 to 1.03), and lung cancer patients (odds ratio: 1.01, 95% confidence interval: 0.94 to 1.00).

Conclusion: Polygenic risk scores may predict the risk of developing cancer, but not the risk of late radiotherapy toxicity. Further research is needed to determine the utility of this score for predicting the risk of late radiotherapy toxicity.
Results: In 2013, a total of 1033 CT examinations were performed in 763 children (424 boys and 339 girls). Of the 1033 examinations, the main target site was the brain/head and neck in 31.6%, followed by the thorax (17.6%), abdomen (16.9%), and bone/soft tissue (13.6%). Traumatic injuries were the reason for undergoing CT in 9.8% (101 of 1033 examinations; 95% confidence interval, 8.0-11.6%). Among the 763 children, 66.1% underwent repeat CT after the first examination, and 19.3% underwent CT eight times or more. Among all examined children, 8.8% had cancer and 4.7% had cancer-prone conditions such as Down syndrome, tuberous sclerosis, and cirrhosis. Only 11.4% of the 763 children underwent CT because of trauma. The rate of trauma decreased with an increase in the frequency of CT examinations. As many as 32.2% of the children had some types of congenital anomaly.

Conclusion: Since the incidence of congenital anomalies is below 2.5% in the general population, it was concluded that the population of children undergoing CT is completely different from that not undergoing CT. It was reported that children with birth defects had a higher risk of cancer compared with children without birth defects, with a relative risk estimated to be approximately 3.0. The two groups should not be compared.


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Liquid Biopsy using “Cell — Free DNA” as Predictive Marker of Response after Radiotherapy in Solid Tumors

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Purpose/Objective(s): The use of “Liquid biopsy” using circulating cell-free DNA (cfDNA) is gaining importance as predictive marker for monitoring treatment outcome in cancer patients. We investigated the clinical significance of cfDNA monitoring in patients with solid tumors treated with radiotherapy (RT).

Materials/Methods: Twenty patients aged 37-74 yrs (median age 55.5yrs) diagnosed with advanced/ metastatic cancers, on RT were recruited in an IRB-approved prospective study. Blood samples were collected before starting RT (T1), during RT (T2) and 30 and 60 days after RT (T3 and T4 respectively). The cohort comprised of 6 Lung, 4 stomach, 4 cervical and 6 breast cancer patients. The cfDNA was purified using a QIAamp Circulating Nucleic Acid Kit (Qiagen, Valencia, CA, and USA) and was quantified and the quality was established using an ALU-based qPCR assay on an AriaMax Real—time PCR System (Agilent, USA).

Results: The cfDNA levels ranged from 1.2-14 ng/ml pre-RT and 2.5-68 ng/ml post RT. Optimal cut-off values for cfDNA were set at 10ng/ml. pre-RT and 15ng/ml post RT to stratify patients into low DNA (LDNA) and high- DNA (HDNA) groups. The pre-RT HDNA in the cohort presented with more advanced and metastatic disease. Quantitative analysis showed that the cfDNA load initially increased significantly post-RT in some patients which correlated with their good treatment outcomes as regression in tumor and disease burden as per the PET-CT scan results.

Since, total cfDNA is derived by cell death associated with apoptosis and necrosis, the increase in cfDNA post RT could be due to more cell death indicating good response to RT. This effect was dose - dependent. On follow up after 2-2.5 months post completion of RT, the cfDNA levels reduced significantly with a good outcome. On the contrary, patients not showing any change in the cfDNA load post RT had less response and a progressive disease confirming a poor response to RT. Case1: A significant change in cfDNA load was seen in a 51 yr old male with small cell neuroendocrine Lung cancer, with brain metastases and pre RT HDNA which increased even after RT doses of 1500 cGy (mid treatment) and 3000 cGy(total dose) to brain . A follow up after 2.5 months post radiation, the cfDNA level came down significantly with a symptomatic reduction of the disease burden in the brain and correlated with clinical response (CR) as shown in PET scan (SUV changed from 15 to Nil).

Conclusions: The study confirms the feasibility and importance for the use of post —RT cfDNA levels as an early predictor of treatment responses for patients with solid tumors in our cohort.


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To Study The Role Of Pre-treatment MicroRNA Expression As A Predictor Of Response To Chemoradiation In Locally Advanced Cervica Cervix

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Purpose/Objective(s): Cervical cancer is the fourth most common cancer worldwide. External beam radiotherapy with concurrent cisplatin followed by brachytherapy is considered standard of care in locally advanced carcinoma cervix, with 50% of patients presenting with recurrence or persistent disease. At present there is no prognostic factor to predict the outcome of disease in locally advanced carcinoma cervix patients treated with standard therapy. MicroRNAs(miRNAs) are small, single stranded noncoding RNA constituting 18-22 nucleotides. It has been shown that miRNAs are differentially expressed (upregulated or downregulated) in many cancer cells. Expression of miRNAs can be used as molecular biomarkers to predict clinical response in locally advanced carcinoma cervix patients.

Materials/Methods: In an observational study, we enrolled 32 patients of locally advanced carcinoma cervix (Stage IB- IVA) after pathological confirmation of biopsy sample from 2017-2018. Expression of six microRNA (miRNA-9 5p, miRNA-31 3p, miRNA-100 5p, miRNA-125a 5p, miRNA-125b-5p, miRNA-200a 5p) in formalin fixed paraffin embedded (FFPE) biopsied tissue were analyzed by real time quantitative reverse transcriptase polymerase chain reaction (RT qPCR). Pre-treatment evaluation of disease status was done with clinical examination and MRI pelvis imaging. All patients received external beam radiotherapy with concurrent chemoradiotherapy followed by brachytherapy as standard treatment. Patients were evaluated for clinical response after 3 months of completion of treatment, with clinical examination and MRI pelvis scan using RECIST 1.1 criteria. Responses were classified as complete response (CR) as disappearance of all disease in response to treatment and Non-response (NR) as patients with partial response, stable or progressive disease. Results were statistically analyzed using Mann Whiney U test to examine significant difference between expression of microRNA between patients with complete clinical response (CR) and those with non-response (NR).

Results: Out of total 32 patients, 24 patients (75%) had Complete Response and 8 patients (25%) had Non-Response to standard therapy. Out of six miRNAs, expression of miRNA-100 5p was upregulated in complete responders (CR) and downregulated in Nonresponders (NR), which showed a trend towards statistical significance (p value = 0.05). Other