Plasma miRNAs as biomarkers for radiation-induced cardiac toxicity in Lithuanian lung cancer patients

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Background
Lung cancer is the second most common malignancy and is the leading cause of cancer death in the world, making up 21% of all cancer deaths. Currently, both non-small cell and small-cell lung cancers have various types of treatment, including radiotherapy as one of the main treatment options in all stages of lung cancer. Despite that, thoracic radiotherapy for lung cancer has been linked to an increased risk of cardiac-related morbidity and mortality. However, currently available methods that predict radiation-induced cardiac toxicity (RICT) are suboptimal. Prediction could potentially be improved by the identification of additional biomarkers, such as circulating plasma miRNAs (miRNAs). Changes in plasma miRNA concentration could be a useful, non-invasive liquid biopsy tool for improved risk stratification, personalized treatment planning and radiation dose prescription.

Purpose
The aim of this study was to identify miRNA expression changes in the plasma, taken from lung cancer patients, pre-and post-ionizing radiation treatment, in order to evaluate the effects of treatment on the heart.

Methods
6 miRNAs (miR-1-3p, miR-21-3p, miR-24-3p, miR-29a-3p, miR-34a-3p, miR-222-3p) were tested for abundance changes in lung cancer patient’s plasma samples before and after treatment with ionization. Overall, 10 pairs of plasma samples were collected before and after radiotherapy. miRNA expression was analyzed using reverse transcription quantitative PCR technique. Cel-miR-39-3p was chosen as exogenous normalization control.

Results
MiR-1-3p, miR-21-3p, miR-24-3p, miR-29a-3p and miR-222-3p were downregulated and miR-34a was upregulated in lung cancer patient’s plasma after radiation therapy when compared to pre-treatment values, but none of them showed significant differences. Nevertheless, before treatment, patients with cardiovascular diseases and higher natriuretic peptide serum concentration values had higher miRNAs relative abundance and showed significant differences compared to the norm of these indicators.

Conclusion
Identification of miR-1-3p, miR-21-3p, miR-24-3p, miR-29a-3p, miR-34a-3p and miR-222-3p levels in lung cancer patients could be used to predict RICT and determine personalized ionization dose to reduce toxicity to the heart. To validate these miRNAs as potential biomarkers for radiation-induced cardiac toxicity further analysis is needed.

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