PO1839

Plasma Proteins Associated with eGFR and Incident Cardiovascular Events in the Cardiovascular Health Study Cohort

Christine P. Limontet,1 Pranav S. Garimella,2 Robert Geserits,3 Diana I. Jalal,3 Michelle Odden,2 Michael Shlipak,1 Nisha Bansal,1 Thomas R. Austin,1 Ian H. de Boer.1

Background: Proteomics may help identify mechanisms through which low estimated glomerular filtration rate (eGFR) increases risks of heart failure (HF), myocardial infarction (MI), and cardiovascular (CV) death. Proteins significantly associated with eGFR were identified using linear regression models. A Bonferroni-corrected p-value less than 7.6x10^-6 was used to account for multiple testing. Proteins significantly associated with eGFR were tested for associations with incident HF, MI, and CV death using Cox-proportional hazard regression adjusting for demographic and clinical variables. We evaluated whether proteins mediated associations between eGFR and incident CV events.

Methods: We utilized an aptamer-based assay to measure 1300 proteins among 3185 older adults in the Cardiovascular Health Study. Proteins associated with eGFR were identified using linear regression models. A Bonferroni-corrected p-value less than 7.6x10^-6 was used to account for multiple testing. Proteins significantly associated with eGFR were tested for associations with incident HF, MI, and CV death using Cox-proportional hazard regression adjusting for demographic and clinical variables. We evaluated whether proteins mediated associations between eGFR and incident CV events.

Results: The mean baseline eGFR was 70 ml/min/1.73m^2 and over a follow-up median of 13 years, there were 1033 incident HF, 555 incident MI, and 963 CV death events. 797 proteins were significantly associated with eGFR. Of these, 52, 0, and 22 proteins were associated with incident HF, MI, and CV death, respectively. The 10 proteins most strongly associated with both HF and CV are shown in Table 1.

Conclusions: eGFR is associated with a large number of plasma proteins. A subset of these proteins are also associated with incident HF and CV death and may reflect mechanisms through which reduced eGFR increases the risk of these outcomes.

Funding: Other NIH Support - NIH NHI.

PO1841

The Impact of Calcification on Intraplaque Hemorrhage in Coronary Atherosclerosis from Autopsy Samples: The Hisayama Study

Toshiaki Nakano,1 Hiromasa Kitazono,1 Yoshinao Oda,1 Takaranai Kitazono,1,2 Kenichi Ishizawa,1 Mika Ochiai,1 Emiko Yuya,1 Garimella Fumika,1 Daigoro Shibata,1 Toshiaki Daigoro,1 Arai Akiyoshi,1,2 Nederlands Kanker Instituut, Amsterdam, Netherlands.

Background: Accelerated coronary artery atherosclerosis is a common complication of thoracic radiation therapy as result of unintended direct cardiac radiation. It is unclear however whether specific areas of the heart are more susceptible to the effects of radiation. In this study we hypothesize that accelerated development of atherosclerotic lesions post radiation (RT) is dependent upon differential sensitivity of specific areas of the heart to the effects of RT.

Methods: Male Apolipoprotein E knockout mice on a high fat diet received 16Gy cardiac RT targeted to the whole or partial (apical or basal) region of the heart at 9 or 16 weeks of age (n=5 per group). Atherosclerotic lesions in H&E stained slides and inflammatory infiltrates in the hearts by IHC were assessed 8 weeks following radiation and compared to unirradiated controls.

Results: Our studies show that(1) Subendocardial atherosclerotic lesions at the base of heart in mice irradiated at 9 weeks of age after basal irradiation are comparable to whole heart irradiation. (2) A greater number of atherosclerotic lesions were present in the basal coronary arteries and basal subendocardial vasculature after irradiation of the cardiac base as compared to unirradiated controls in mice irradiated at 16 weeks of age (Table). (3) Apical or whole heart irritation had no impact on the development of lesions in the basal region of the hearts of 16 week old mice (Table). (4) IL-6 was significantly increased in the serum of mice 6 hours post basal cardiac irradiation (105.10±17.56 pg/ml) when compared to unirradiated controls (29.85±11.63 pg/ml) demonstrating an early inflammatory response. (5) Infiltration of inflammatory cells (CD45, CD68) and expression of endothelial adhesion molecules (CD31) were differentially and locally regulated based upon the site of irradiation.

Conclusions: Our results indicate that the base of the heart is more prone to development of RT induced atherosclerotic lesions likely due to acute and delayed inflammatory responses. Avoiding this area from direct radiation exposure may improve the quality of life for cancer patients receiving thoracic RT.