P0669 **HIGH ESTIMATED PHENOTYPIC AGE ASSOCIATES WITH WORSE CLINICAL OUTCOME IN CHRONIC KIDNEY DISEASE PATIENTS**

Hokuto Morohoshi[1,2], Ken Iseri[1,3], Lu Dai[1], Thomas Ebert[1], Anna Witasp[1], Bengt Lindholm[1], Olof Heimbürger[1], Franz Peter Barany[1], Louise Nordfors[1], Karolina Kublickiene[1], Abdul Rashid Tony Qureshi[1], Paul Shiels[4], Peter Stenvinkel[1]

[1]Karolinska Institutet, Division of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Stockholm, Sweden, [2]Showa University, Clinical Research Institute for Clinical Pharmacology & Therapeutics, Tokyo, Japan, [3]Showa University School of Medicine, Division of Nephrology, Department of Medicine, Tokyo, Japan and [4]Institute of Cancer Sciences, University of Glasgow, Wolfson Wohl Cancer Research Center, Glasgow, United Kingdom

Background and Aims: Ageing represents the greatest risk factor contributing to increased morbidity and mortality in most chronic diseases; it encompasses numerous biological changes resulting in declining physiological function and increasing burden of disease. Whether new biomarkers of ageing and risk scores for predicting physiological outcomes, including mortality, are applicable and more accurate than chronological age in patients with chronic kidney disease (CKD) is not clear. So far, the DNA methylation (DNAm) PhenoAge biomarker of ageing (Levine et al. Aging 2018) has not been tested in CKD. While we had no access to DNAm data, we applied the phenotypic age estimate proposed by Levine et al., which was included in their calculations of DNAm PhenoAge, and tested the relationship between estimated phenotypic age (ePhenoAge) and chronological age, respectively, with all-cause mortality in patients with CKD.

Method: In a cohort of 333 CKD patients (stage 1, n=78; stage 3-4, n=64; and stage 5, n=191) with median age 56 years, 43% females, 24% diabetes (DM), 25% cardiovascular disease (CVD), and 22% malnourished, we estimated age by ePhenoAge, using a formula with calculations based on nine biomarkers and chronological age, and compared this age index with chronological age. Framingham risk score, body composition, nutritional status, handgrip strength, and various biochemical markers (white blood cells, mean cell volume, hemoglobin, albumin, creatinine, glucose, calcium, alkaline phosphatase, intact-parathyroid hormone, triglyceride, cholesterol, HDL-cholesterol, high-sensitivity C-reactive protein (hsCRP), and interleukin (IL)-6) were recorded. During a median follow-up period of 52 months, 65 patients died, and 111 patients underwent renal transplantation. We used spline curve to illustrate sub-distribution hazard risk (sHR) for all-cause mortality versus increasing ePhenoAge and chronological age respectively as obtained by the Fine and Gray competing risk analysis.

Results: In univariate analyses, IL-6 (rho=0.49, $p<0.001$; n=268) and hsCRP (rho=0.37, $p<0.001$; n=333) were significantly correlated with ePhenoAge. The ePhenoAge remained significantly associated with hsCRP ($p=0.02$) when adjusted for sex, DM, CVD, nutritional status and CKD stages. The spline curves showing sHR for all-cause mortality derived from multivariate competing risk analysis and adjusted for sex, presence of DM and CVD, hsCRP, nutritional status and CKD stages, showed increased mortality risk with higher chronological age (sHR: 1.08, $p<0.001$). In contrast, the association of mortality with higher ePhenoAge (sHR: 1.04, $p=0.06$) was of borderline statistical significance.

Conclusion: All-cause mortality risk was associated with increasing chronological age in competing risk analysis with adjustments of confounders. A similar trend was observed for ePhenoAge, a finding which to a large extent may be explained by the inflammatory status of the study subjects. However, contrary to expectations, ePhenoAge was not as powerful as chronological age in predicting mortality, underlining that our knowledge about factors influencing phenotypic age in CKD patients is still limited. This should motivate further study of the potential role of other estimates of biological age in CKD.