SP012 A POLYMORPHISM IN THE SIRT-1 GENE ASSOCIATES WITH CONCENTRIC REMODELLING OF THE LEFT VENTRICLE AND PREDICTS THE LONGITUDINAL EVOLUTION OF THIS ALTERATION BOTH IN STAGE G1-5 CKD PATIENTS AND IN DIALYSIS PATIENTS

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INTRODUCTION AND AIMS: Left ventricular hypertrophy and concentric remodeling of the left ventricle (LV) is a hallmark of chronic kidney disease (CKD). The Silent Information Regulator gene 1 (Sirt1) belongs to a family of NAD^+-dependent protein deacetylases involved in a wide range of biologic processes, including inflammation, oxidative stress and nitric oxide synthesis, which are altered in CKD. Sirt1 promotes cardiomyocyte growth under stress conditions and therefore polymorphisms in the gene regulating this protein may be involved in the geometric remodeling of the LV in CKD.

METHODS: We investigated the cross-sectional and longitudinal relationship between three candidate polymorphisms in the Sirt1 gene (i.e. rs7895833 A>G, rs7069102 C>G and rs2273773 C>T) and LV mass and geometry (LV mass-to-volume ratio) in two cohorts of CKD patients including 179 Greek stage G1-5 CKD patients maintained on conservative treatment and 235 Italian patients on chronic dialysis (stage G5D).

RESULTS: In the cross-sectional analysis, the Sirt1 rs7069102 polymorphism (dominant model: CC/CG versus GG) coherently associated with LV mass-to-volume ratio in the two study cohorts both in unadjusted and adjusted analyses (*Greek cohort*, beta=0.15, P=0.048; *Italian cohort*, beta=0.16, P=0.017) but neither with LV mass nor with LV volume. In longitudinal analyses by linear mixed models including baseline and repeated LV mass-to-volume ratio measurements as dependent variable (1186 measurements over a follow up extended up to 36 months), patients with CC/CG genotype showed an increase in LV mass-to-volume ratio over time which was significantly higher than that observed in patients with GG genotype and this difference was statistically significant and of similar magnitude in the two cohorts both in unadjusted (*Greek cohort*, regression coefficient=0.14, 95%CI: 0.02-0.26; P=0.02; *Italian cohort*, regression coefficient=0.14, 95%CI: 0.003-0.287; P=0.045) and adjusted analyses (*Greek cohort*, regression coefficient=0.13, 95%CI: 0.01-0.26; P=0.037; *Italian cohort*, regression coefficient=0.15, 95%CI: 0.01-0.29; P=0.003). Neither the rs7895833 A>G nor the rs2273773 C>T polymorphism associated with LV mass or LV geometry.

CONCLUSIONS: The rs7069102 polymorphism in the Sirt1 gene associates with concentric remodeling of the left ventricle both in stage G1-5 pre-dialysis patients and in stage G5 CKD patients maintained on chronic dialysis. Longitudinal analyses also document that the same polymorphism coherently predicts the evolution of concentric remodeling in the same patients. These results provide a genetic basis to the hypothesis that the Sirt1 gene plays an important role in LV remodelling in patients with CKD of various severity.