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P033 -Association analysis of SNPs on Chromosome Y in renal disease in two cohorts.

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Chronic kidney disease (CKD) affects approximately 10-15% of the global population and is a major public health problem, with up to £1.4 billion of the annual NHS budget devoted to renal disease and its complications each year. Earlier diagnosis of CKD could allow the implementation of preventative measures, but current methods for recognising CKD (serum creatinine; eGFR; urinary albumin excretion) only allow detection of kidney disease once pathological damage is present. Novel biomarkers are required to allow identification of individuals at high risk of CKD before renal function becomes impaired. Single nucleotide polymorphisms (SNPs) and other genomic variants could be useful as potential biomarkers for CKD. Most SNP-based studies of renal disease have only investigated autosomal SNPs and exploration of chromosome Y variants remains limited. Chromosome Y SNPs are associated with coronary artery disease, a condition closely linked with CKD. Furthermore, men with CKD tend to progress to end-stage renal disease (ESRD) faster than women do, providing further justification for study of chromosome Y genetics in CKD. High-quality DNA was used from a subset of individuals in two populations. Individuals with type 1 diabetes and diabetic kidney disease (DKD) and diabetic controls without renal disease were employed from the GENetics of Nephropathy: an International Effort (GENIE) consortium. The Wellcome Trust Case Control Consortium 3 Belfast cohort (WTCCC3) consisted of kidney transplant recipients with ESRD and kidney transplant donors with no kidney disease as controls. Samples were genotyped using the Illumina HumanOmni1-Quad array (GENIE) and the Illumina 670 Quad Custom array (WTCCC3). After quality control procedures, 304 DKD patients and 390 controls from GENIE, and 156 ESRD patients and 136 controls from WTCCC3 remained. In the GENIE and WTCCC3 cohorts, 483 SNPs and 8 SNPs passed quality control, respectively. Age-adjusted association analysis using logistic regression was performed for each phenotype (DKD for GENIE; ESRD for WTCCC3). SNPs common to both cohorts (n=4) were then meta-analysed. No chromosome Y SNPs were significantly associated with DKD in the GENIE cohort. Two SNPs, rs2032621 (OR: 0.1) and rs2032590 (OR: 0.1) in the WTCCC3 cohort reached the Bonferroni-corrected significance threshold for ESRD ($p < 0.0167$), but were not included in the meta-analysis as these SNPs were only present in the WTCCC3 cohort. None of the four SNPs included in the discovery meta-analysis reached significance. The small odds ratios for rs2032621 and rs2032590 is likely due to a low minor allele count in this sample (n=6), and therefore would need further confirmation in a larger population. The relatively low number of individuals included in the study also limits power of the analysis, but all samples used represent the only UK/ROI data with sufficient information available for publication at this time. Of note, this is the largest report of association analysis on chromosome Y for renal disease in to date. Chromosome Y genetic variants may play a role in the faster progression of CKD and higher ESRD prevalence in men. The limited chromosome Y SNP representation on commercially available genotyping arrays is limiting further study of this hypothesis.