OP-0134 – SNPs in *PRKCA-HIF1A-GLUT1* are associated with diabetic kidney disease in a Chinese Han population with type 2 diabetes

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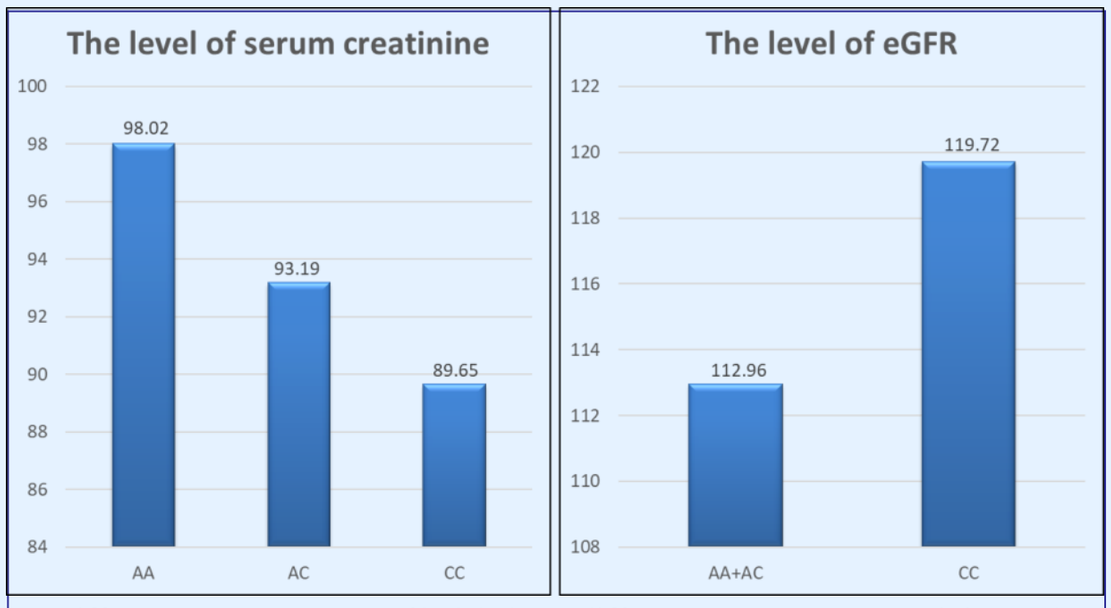
BACKGROUND: Diabetic kidney disease has been confirmed to have genetic underpinnings. Diabetes complications depend on abnormal intracellular glucose accumulation transferred by glucose transporters. Studies have shown that the glucose transporter 1 (*GLUT1*) allele (XbaI–) is associated with nephropathy in type 2 diabetes. The association of hypoxia-inducible factor 1A (*HIF1A*) and diabetic kidney disease has been reported. Protein kinase C alpha (*PRKCA*) inhibitors have been a focus of research on diabetic kidney disease treatment. Moreover, there is evidence showing that *PRKCA*, *HIF1A* and *GLUT1* are located in a pathway closely related to hypoxic-related kidney injury. Therefore, we carried out this experiment to explore the relationship between SNPs in *PRKCA-HIF1A-GLUT1* and diabetic kidney disease in Chinese Han people.



Different genotypes at rs1681851 have different mean serum creatinine and eGFR

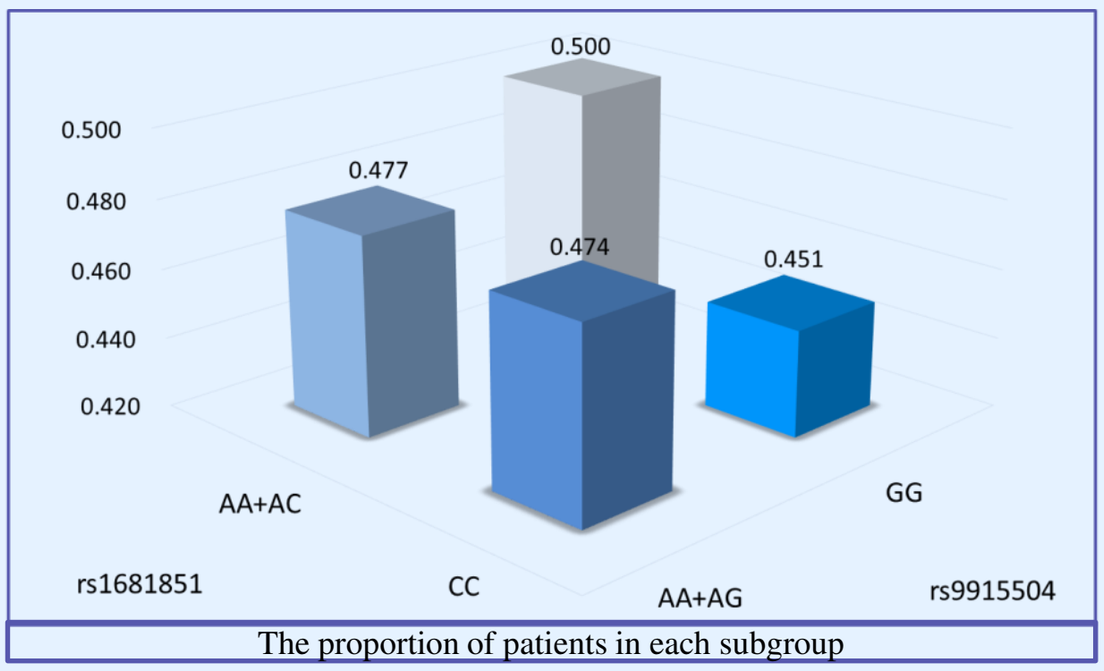
CHR	*SNP*	*Position*	*Gene*	*Allele*	*MAF*	*Model*	*OR*	*SE*	*P*	*Model*	*OR*	*SE*	*P*
1	rs1681851	42923357	*GLUT1*	A/C	0.4934	1	1.149	0.0690	**0.0443**	2	1.104	0.0747	0.1846
						3	1.331	0.1118	**0.0105**	4	1.084	0.1141	0.4780
14	rs2301108	61730746	*HIF1A*	A/G	0.1754	1	1.169	0.0884	0.0771	2	1.289	0.0964	**0.0085**
						3	1.222	0.1058	0.0580	4	1.139	0.2495	0.6011
14	rs116908431	61738919	*HIF1A*	G/T	0.0529	1	1.048	0.1537	0.7610	2	1.101	0.1681	0.5679
						3	1.079	0.1584	0.6317	4	0.289	1.1860	0.2956
14	rs79865957	61744249	*HIF1A*	T/G	0.1594	1	1.128	0.0923	0.1919	2	1.263	0.1007	**0.0204**
						3	1.179	0.1078	0.1262	4	0.998	0.2788	0.9929
17	rs9915504	66794316	*PRKCA*	A/G	0.3359	1	0.894	0.0723	0.1222	2	0.919	0.0787	0.2813
						3	0.821	0.0984	**0.0446**	4	0.978	0.1512	0.8833

Association with the occurrence of DKD in stage 1

METHODS: A total of 2552 participants from Shanghai Diabetes Institute Inpatient Database of Shanghai Jiao Tong University Affiliated Sixth People's Hospital were involved in the stage 1 cross-sectional population. A total of 6015 subjects from the Hong Kong Diabetes Register were included for validation. Genotyping of participants was conducted by the MassARRAY Compact Analyzer (Agena Bioscience, San Diego, CA, USA). The data was analyzed by plink, SAS, Haploview.

RESULTS: We identified variants associated with diabetic kidney disease in stage 1. Rs1681851 (P=0.0105, OR=1.331) in *GLUT1* as well as rs2301108 (P=0.0085, OR=1.289) and rs79865957 (P=0.0204, OR=1.263) in *HIF1A* were significantly associated with diabetic kidney disease. Regarding DKD-related traits, rs1681851 was associated with plasma creatinine levels (P=0.0169, beta=4.822) and eGFR (P=0.0457, beta=-6.956). Moreover, the results showed the interactions between *PRCKA-GLUT1* in the occurrence of DKD. We further sought validation of the 8 suggestive SNPs in a prospective cohort and found that rs900836 was associated with the percentage change in eGFR slope. We performed a meta-analysis of case-control analysis data from the Hong Kong samples together with the stage 1 data from Shanghai. No SNP reached statistical significance in the meta-analysis.

CONCLUSION: Our results suggest potential association between SNPs in *PRKCA-HIF1A-GLUT1* and diabetic kidney disease in Chinese Han people.



The proportion of patients in each subgroup

CHR	*SNP*	*Position*	*Gene*	*Allele*	*MAF*	*OR*	*SE*	*P*
1	rs900836	42947056	*GLUT1*	T/C	0.229			
			Original eGFR slope			-0.06	0.05	0.2026
			eGFR slope percentage			-0.25	0.11	**0.0308**

Association with eGFR slope in prospective cohort