The coronary artery disease SNP, rs4420638, is associated with diabetic nephropathy rather than end-stage renal disease

Sir,

We recently reported the genetic analysis of coronary artery disease single nucleotide polymorphisms (SNPs) in type 1 diabetic patients with and without diabetic nephropathy [1]. A novel and statistically significant association was observed between a SNP and diabetic nephropathy (rs4420638; \(P_{\text{corrected}} = 0.002\)). This finding was subsequently replicated in a phenotypically similar case–control collection with type 1 diabetes from the British Isles. In our original report, 27% of the diabetic nephropathy cases had end-stage renal disease (ESRD). We have now sought to clarify if this SNP (rs4420638) was specifically associated with diabetic nephropathy or whether it was associated instead with ESRD, by assessing a further reasonably well-powered case-control collection where all the cases had ESRD. Biological and epidemiological data support genetic susceptibility to ESRD as evidenced by familial clustering of renal failure [2], different prevalence rates in distinct ethnic populations [3] and genetic variants modifying progression [4].

Ethical approval (www.orecni.org.uk) was obtained prior to conducting this study. Patients with ESRD receiving their first renal allograft \((n = 645)\) were defined as cases, and their respective deceased kidney donors \((n = 554)\) were the control group. All patients were Caucasian. Recipients had a primary cause of renal disease recorded and classified according to the European Dialysis and Transplant Association coding system (www.era-edta.org). The most common causes of ESRD were glomerular disease (21%) and pyelonephritis/interstitial nephritis (20%); fewer than 10% had diabetic nephropathy. Genotyping was performed for rs4420638 using the MassARRAY iPLEX™ assay (Sequenom, San Diego, CA, USA) and statistical analysis conducted as previously described for the case–control collection [1]. Genotyping in the renal transplant population had a success rate of 99.7% with a minor allele frequency of 15%.

In summary, this further research suggests that the coronary artery disease SNP, rs4420638, is associated with diabetic nephropathy rather than ESRD. It will be of interest to try and replicate this finding in a very large type 1 diabetic cohort to try and distinguish between genetic susceptibility to cardiovascular disease versus diabetic nephropathy.

Conflict of interest statement. None declared.

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The role of fructose in inducing metabolic syndrome is speculative

Sir,

The conclusion in the Editorial Review by Cirillo et al. [1] that excessive intake of fructose may have a key role in