Definitions

The world health organization (WHO) 1995 classification system [1] was used for the classification of renal biopsies, where mesangial nephritis was defined as class I-II, proliferative nephritis as class III-IV, membranous nephritis as class V. Patients with biopsies displaying signs of nephritis but not meeting the criteria for any of the above classes, [1] were classified as *other*. Patients who had undergone renal transplantation or were receiving dialysis were considered to have end-stage renal disease (ESRD). dsDNA positivity was defined according to the ACR-82.[2]

A clinical diagnosis of APS was made based on thrombotic events and/or miscarriage in combination with positive tests for IgG aCL, IgG aß$_2$GPI or LA, and classified according to Miyakis *et al.*[3] Triple-positivity for aPL was defined as having positive tests for aCL (IgG or IgM) and aß$_2$GPI (IgG *or* IgM) and LA. Myocardial infarction (MI) required confirmation by electrocardiography and a rise in plasma creatine kinase, muscle and brain fraction (CK-MB) or troponine T, and ischemic cerebrovascular disease (ICVD) by computer tomography or magnetic resonance imaging. Venous thromboembolism (VTE) was defined as deep vein thrombosis, confirmed by venography or ultrasonography, and/or pulmonary embolism, confirmed by radionuclide lung scanning or angiogram.

Genotyping and quality control

Genomic DNA was extracted from peripheral blood of SLE patients from both the discovery and replication cohorts by using Qiagen Blood Midi Kit (Qiagen, Hilden, Germany. The discovery cohort and healthy controls were genotyped with the Illumina 200K Immunochip SNP array at the SNP&SEQ Technology Platform at Science for

Life Laboratory in Uppsala, Sweden. Quality control was performed sample-wise and SNP-wise. Clustering and genotype calling was performed using Illumina's GenCall software. Sample call rate below 95% and SNPs with call rate below 100% were excluded. Samples with abnormal autosomal heterozygosity rate with more than 5SD from the mean of Wright's inbreeding coefficient F were excluded. A check for mislabelled gender was performed using Wright's inbreeding coefficient F, calculated from X chromosome data. Annotated females with F close to one or annotated males with F close to zero were excluded. Cryptic relatedness was analysed using KING software[4] and one sample from each related pair (up to 2nd degree of relatives) was excluded. Furthermore, principal component analysis (PCA) was performed on 1000 Genomes Project data and then used to project and exclude study samples falling more than 5SD from European populations in each of 5 principal components. SNPs with minor allele frequency (MAF) < 1% or with Hardy-Weinberg equilibrium (HWE) p-values within FDR < 5% (based on controls only) were excluded, described in [5].

Genotyping of the replication cohort was performed using the iPLEX chemistry on a MassARRAY system (Agena Bioscience, San Diego, CA, USA). QC included a minimum per sample call rate of 90% and a per variant call rate of 90%. 836 Norwegian and Danish SLE patients passed QC.

References

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