Electronic supplementary material

Methods

Cohort selection of UKPDS antibody-positive patients and comparison of GADA assays

Autoantibody measurements in samples taken at diagnosis GADA status at diagnosis was determined in UKPDS patients using a GADA porcine assay as described previously [1–3] with values $\geq$20 units/ml considered positive according to the Juvenile Diabetes Foundation (JDF) 1995 workshop (here termed GADA\textsubscript{JDF}). ICA and IA-2A positivity was also determined in these samples [3, 4]. The patients included in the current study were selected as described in ESM Fig. 1.

To ensure that data from the radiobinding assay, which was validated in the DASP workshop (here termed GADA\textsubscript{DASP}-positive), were identifying a representative subset ($n=242$) of the original antibody-positive cohort (GADA\textsubscript{JDF}-positive) ($n=443$) (ESM Fig. 1) a comparison of the clinical details of the cohorts was made. These data are shown in ESM Table 1. GADA\textsubscript{DASP}-positive patients were similar to the GADA\textsubscript{JDF}-positive patients with respect to age, sex and HOMA %S but had higher mean HbA\textsubscript{1c}, lower HOMA %B, systolic BP and plasma triacylglycerols, and less often had the metabolic syndrome. The clinical characteristics at diagnosis of this subgroup of 242 GADA\textsubscript{DASP}-positive patients suggested that they represented a more precise clinical and biochemical delineation of LADA patients compared with the overall autoantibody-positive UKPDS LADA group previously reported [3]. Similarities between the patient characteristics indicate that the cohort of 242 patients can be considered a representative sample of all the UKPDS autoantibody-positive patients identified with the GADA\textsubscript{JDF} assay.

Comparisons of GADA\textsubscript{JDF} and GADA\textsubscript{DASP} levels at diagnosis/0.5 years, 3 years and 6 years Changes in GADA\textsubscript{JDF} levels over time were determined in a subset of UKPDS patients who were GAD\textsubscript{JDF} autoantibody-positive at diagnosis. Plasma samples taken 3 and 6 years after diagnosis were assayed in 90/526 patients who were chosen at random (ESM Fig. 1). GADA\textsubscript{JDF} positivity persisted in the majority with Spearman rank correlation coefficients for levels at 3 and 6 years of 0.76 ($p<0.0001$) and 0.72 ($p<0.0001$), respectively. At 3 and at 6 years after diagnosis, 65 and 59 patients, respectively, remained GADA\textsubscript{JDF}-positive.
Seroconversion to positivity was assessed in a further 166 patients who were GADA_{JDF}-negative at diagnosis and matched for age, sex and BMI with the GADA_{JDF} autoantibody-positive at diagnosis cohort. Of these, one patient was designated GADA_{JDF}-positive at both 3 and 6 years and two patients positive at 6 years.

To ensure that selection of the two cohorts based on the two different assays was consistent, comparisons were made of the GADA data for as many patients who were included in the GADA_{DASP}-positive (at 0.5 years) cohort and tested at diagnosis and at 3 and 6 years by the GADA_{JDF} assay (ESM Fig. 2). There were close correlations between GADA_{DASP} levels (WHO units/ml) at 0.5 years and GADA_{JDF} levels (JDF units/ml) at diagnosis and at subsequent time-points; the Spearman rank correlation coefficients were: GADA_{DASP} 0.5 years vs GADA_{JDF} at diagnosis 0.62, \( p<0.0001, n=242 \); GADA_{DASP} 3 years vs GADA_{JDF} 3 years 0.74, \( p<0.0001, n=69 \); GADA_{DASP} 6 years vs GADA_{JDF} 6 years 0.74, \( p<0.0001, n=64 \). These different data taken together suggest that both assays identify a similar range of GADAs in LADA patients soon after diagnosis and at later time points.

References


