UKPDS 25: autoantibodies to islet-cell cytoplasm and glutamic acid decarboxylase for prediction of insulin requirement in type 2 diabetes. UK Prospective Diabetes Study Group.

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BACKGROUND: Autoantibodies to islet-cell cytoplasm (ICA) and glutamic acid decarboxylase (GADA) can occur in apparently typical, non-insulin dependent diabetes mellitus (type 2). We investigated whether the presence of either or both antibodies characterises a subtype of diabetes and provides better prediction of requirement for insulin therapy by 6 years' follow-up than clinical variables. METHODS: We measured ICA and GADA at diagnosis of diabetes in a representative population of 3672 white patients with type 2 diabetes, aged between 25 and 65 years. The phenotype was assessed by age of onset, body-mass index, percentage haemoglobin A1c (HbA1c), and islet beta-cell function. We investigated the need for insulin therapy among 1538 patients not assigned insulin and followed up for 6 years from diagnosis. FINDINGS: The proportion of patients with ICA and GADA decreased with increasing age at diagnosis (from 33 [21%] of 157 patients aged 25-34 [corrected] to 66 [4%] of 1769 aged 55-65 for ICA; from 53 [34%] to 122 [7%] for GADA). Among patients younger than 35 at diagnosis, those with ICA or GADA had lower body-mass index than those without (mean 24.9 [SD 6.0] vs 31.7 [7.3] kg/m2; $p < 0.0001$ and had higher percentage of HbA1c (9.7 vs 8.7%, $p < 0.05$). 94% of patients with ICA and 84% of those with GADA required insulin therapy by 6 years, compared with 14% of those without the antibodies ($p < 0.0001$). Among patients older than 55 at diagnosis, the difference between those with and without antibodies in body-mass index was smaller (27.2 [5.4] vs 28.6 [4.8] kg/m2, $p < 0.001$); 44% of those with ICA, 34% of those with GADA, and 5% with neither antibody required insulin therapy by 6 years ($p < 0.0001$). Among patients older than 45 years, body-mass index and HbA1c provided little predictive information for insulin requirement, whereas the positive predictive values of GADA (> or = 60 U/L) alone, or both GADA (> or = 20 U/L) and ICA (> 5 U/L), for insulin therapy were 52% and 68%. INTERPRETATION: Among young adults with type 2 diabetes, the phenotype of those with ICA

or GADA antibodies was similar to that of classic juvenile-onset insulin-dependent diabetes, and either phenotype or antibodies predicted insulin requirement. In older adults, the phenotype was closer to that of patients without antibodies and only the presence of antibodies predicted an increased likelihood of insulin requirement.