Risk of microvascular complications over 30 years in latent autoimmune diabetes of adults compared with type 2 diabetes

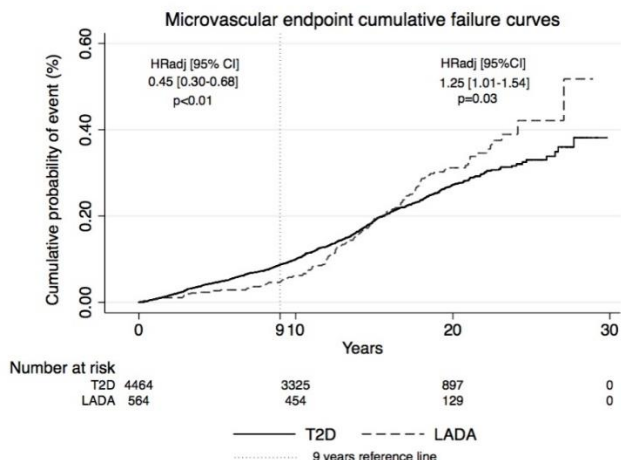E. Maddaloni[1], R.L. Coleman[2], O.F. Agbaje[2], R. Buzzetti[1], R.R. Holman[2];
[1]Sapienza University of Rome, Rome, Italy, [2]Diabetes Trial Unit, University of Oxford, Oxford, UK.

Background and aims: Latent Autoimmune Diabetes of Adults (LADA) is a mild form of autoimmune diabetes diagnosed in 2-12% of adults with a clinical diagnosis of type 2 diabetes (T2D). LADA differs in genetic and clinical features from T2D, but whether this translates into a different risk of microvascular complications remains uncertain. We examined the long-term risk of microvascular complications in the 5102 patients with clinically-diagnosed new-onset T2D enrolled into the United Kingdom Prospective Diabetes Study (UKPDS), according to their LADA status.

Materials and methods: 5028 UKPDS participants who had diabetes autoantibody (AAb) measurements available (ICA, GADA and/or IA-2A) and had no prior microvascular events were included in our study. Those with at least one detectable AAb (n=564) were defined as having LADA. Yearly measurements of HbA_{1c}, fasting plasma glucose and insulin were performed *per* the UKPDS protocol. Homeostasis Model Assessment was used to estimate steady state beta-cell function (HOMA2_%B). Nine-year updated mean HbA_{1c} and HOMA2_%B values were calculated for each participant from annual measurements. We defined a composite microvascular outcome as the first occurrence of renal failure, renal death or diabetic retinopathy (blindness, vitreous haemorrhage or photocoagulation) and compared incidence rates between T2D and LADA.

Results: At diagnosis, LADA participants were younger and more frequently White Caucasian, with lower body mass index, total cholesterol, systolic blood pressure and HOMA2_%B values, and with higher HDL-cholesterol and HbA_{1c} values (p<0.01 for all). After median (IQR) 17.3 (12.6, 20.7) years follow-up, the composite microvascular outcome had occurred in 1041 (20.7%) participants. A time-varying Cox-model adjusted for baseline characteristics showed that LADA, compared with T2D participants, had non-proportional hazards with a lower risk of the composite microvascular outcome during their first 9 years of follow-up (HR_{adj}0.45, 95%CI 0.30-0.68, p<0.01) and a higher risk in subsequent years (HR_{adj}1.25, 1.01-1.54, p=0.03) (Figure). Nine-year updated median (IQR) HbA_{1c} values were higher in LADA compared with T2D participants (8.1% [6.8, 9.3] *vs.*7.1% [6.3, 8.2], p<0.01), whilst nine-year updated median HOMA2_%B values did not differ (60.5% [37.0, 89.8] *vs.*60.8% [42.1 86.8], p=0.47). Nine-year updated median $HbA_{1c}$and HOMA2_%B values were significantly associated with the composite microvascular outcome (P<0.01 for both). When added to the Cox model, updated HOMA2_%B did not alter the HR whereas when updated $HbA_{1c}$was added there was no longer a difference in microvascular risk between LADA and T2D participants (HR_{adj}0.99, 0.80-1.23, p=0.93).

Conclusion: At diabetes onset, patients with LADA initially have a lower risk of microvascular complications compared with T2D, but in the longer term have a higher risk as a consequence of worse glycaemic control.

Microvascular endpoint cumulative failure curves