Risk of cardiovascular disease in individuals with latent autoimmune diabetes of adults: results from the UKPDS

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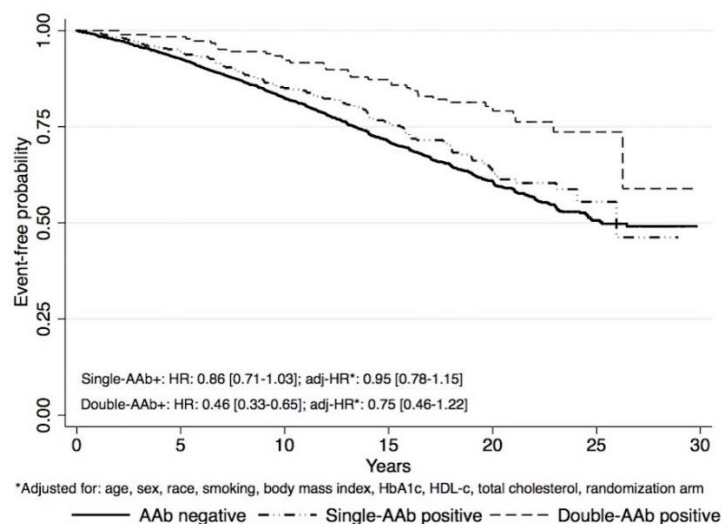[1]Dept of Medicine, Unit of Endocrinology and Diabetes, Campus Bio-Medico University of Rome, Rome, Italy, [2]Diabetes Trial Unit, University of Oxford, Oxford, UK.

Background and aims: Diabetes autoantibodies (AAb) to islet-cell cytoplasm (ICA), to glutamic acid decarboxylase (GADA) or to islet antigen-2 (IA-2A), are detectable in up to 12% of adults with a clinical diagnosis of type 2 diabetes (T2D). The presence of AAb identifies subjects with adult-onset autoimmune diabetes, who are mostly affected by a slowly progressive form known as latent autoimmune diabetes of adults. Subjects with detectable AAb tend to be leaner and to have a healthier cardiovascular (CV) risk profile than AAb-negative subjects, but it remains uncertain whether the risk of CV events differ between these two groups. We examined the long-term risk of CV disease in the large population with a clinical diagnosis of new-onset T2D enrolled in the United Kingdom Prospective Diabetes Study (UKPDS), according to their AAb status.

Materials and methods: ICA, GADA and IA-2A were measured in 5096 UKPDS participants at or soon after diagnosis of T2D. The incidence of major adverse CV events, a composite of cardiovascular death, nonfatal myocardial infarction or nonfatal stroke (MACE3), was compared between those with no antibodies (AAb-) and those with ≥ 1 AAb positive tests (AAb+). Hazard ratios (HR) were adjusted for pre-specified potential confounders (age, race, sex, metabolic profile and smoking status) and for therapy allocation (diet, insulin, sulfonylureas, metformin, non-randomized). The interaction between CV risk factors (age, sex, lipid profile, body mass index [BMI], HbA1c, systolic blood pressure [SBP], smoking status) and AAb status was also examined.

Results: The 557 AAb+ UKPDS participants were younger, with higher mean HbA_{1c} and HDL-cholesterol values but lower BMI, total cholesterol and SBP values than AAb- subjects (all $p<0.01$). Over a mean$\pm$SD follow-up period of 16.3 ± 6.0 years a total of 1071 MACE3 events occurred with incidence rates/1000 person-years (95% confidence interval [CI]) of 17.1 (14.6-20.0) in AAb+ and 23.5 (22.4-24.7) in AAb- participants (HR 0.71, CI 0.60-0.84, $p<0.001$). Following adjustment for pre-specified confounders, there was no significant difference in MACE3 risk between AAb+ and AAb- participants (adj-HR 0.90, CI 0.76-1.07, $p=0.22$). The 186 UKPDS participants with ≥ 2 positive AAb tests (double-AAb+) had the lowest MACE3 risk (HR 0.46, CI 0.33-0.65, $p<0.001$), but this difference became non-significant following adjustment for potential confounders (adj-HR 0.75, CI 0.46-1.22, interaction $p=0.25$) (See Figure). There were no significant interactions between CV risk factors and AAb status.

Conclusion: In adults with newly-diagnosed diabetes the long-term risk of MACE3 does not differ between those with and without detectable AAb after adjustment for confounders. This suggests measurement of diabetes AAb does not aid in the stratification of CV risk among adults with a clinical diagnosis of new-onset T2D.

Single-AAb+: HR: 0.86 [0.71-1.03]; adj-HR*: 0.95 [0.78-1.15]
Double-AAb+: HR: 0.46 [0.33-0.65]; adj-HR*: 0.75 [0.46-1.22]

*Adjusted for: age, sex, race, smoking, body mass index, HbA1c, HDL-c, total cholesterol, randomization arm

——— AAb negative — · — · — Single-AAb positive — — — — Double-AAb positive

Disclosure: **E. Maddaloni:** None.