**Impact of Body Composition on the Relationship Between Insulin Resistance and Cardiometabolic Risk in Type 1 Diabetes**

**Aim**

Insulin resistance is associated with markers of cardiometabolic risk. Fat free mass (FFM) is used to normalise clamp-based measures of insulin resistance as it is considered the most metabolically active tissue. Yet adipose insulin resistance is a key metabolic defect in type 1 diabetes. We compared the strength of associations between insulin sensitivity normalised to total body weight (TBW) versus FFM, and markers of adiposity, glycaemia, and vascular health in a subset of subjects in the RESET1 trial.

**Method**

Whole-body insulin sensitivity was measured using the hyperinsulinaemic-euglycaemic clamp (insulin 60 mUm2/min, target glucose 5.5 mmol/L) in 38 adults with type 1 diabetes (mean age 50 years, HbA1c 7.4%, BMI 32.3 kg/m2, diabetes duration 26 years, 34% female). The clamp M-value (whole body glucose disposal rate) was separately normalised to TBW and FFM. Associations with arterial stiffness (measured by carotid femoral pulse wave velocity (cfPWV)), HbA1c, lipid profile, and visceral adipose tissue (VAT by dual-energy x-ray absorptiometry) were assessed using Spearman’s correlations and linear regression models adjusted for age and sex. Correlation coefficients were compared to assess effect size differences.

**Results**

Using Spearman’s correlations, M/weight showed stronger association with VAT (ρ=-0.56, p=0.0008 vs (ρ=-0.47, p=0.007) and triglycerides (ρ=-0.33, p=0.04 vs ρ=-0.29, p=0.08) compared to M/FFM. In contrast, M/FFM was more strongly associated with HDL cholesterol (ρ=0.40, p=0.01 vs ρ=0.29, p=0.08). HbA1c was not associated with insulin resistance in either measure. When adjusted for age and sex, M/weight showed stronger association with arterial stiffness as measured by cfPWV (β=-0.71, p=0.02 vs β=-0.64, p=0.13) compared to M/FFM.

**Conclusion**

The method of normalisation influences observed associations between insulin resistance and cardiometabolic risk factors in type 1 diabetes. These findings underscore the need to consider body composition when interpreting insulin sensitivity metrics in type 1 diabetes cardiometabolic research.