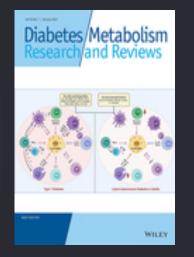
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## ARTICLE

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#### **RESEARCH ARTICLE**

# Estimated insulin sensitivity, cardiovascular risk, and hepatic steatosis after 12 years from the onset of T1D

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Abstract with type 1 diabetes. 0.03 to <0.0001).

Abbreviations: ALT, Alanine aminotransferases; AST, Aspartate aminotransferases; BMI, Body Mass Index; CACTI, Coronary Artery Calcification in Type 1 diabetes Study; CVD, CardioVascular Disease; cIMT, Carotid Intima Media Thickness; DID, Daily insulin dose; eGDR, Estimated Glucose Disposal Rate; EDC, Pittsburgh Epidemiology of Diabetes Complications Study; EMRs, Electronic medical records; elS, Estimated Insulin Sensitivity; HbA1c, Glycosylated haemoglobin; HDL, High density lipoprotein; HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; HS, Hepatic Steatosis; HT, Hypertension; IIT, Intensive Insulin Treatment; IRS, Insulin Resistance Syndrome; ISS, Insulin Sensitivity Score; yGT, y-glutamyl-transferase; LDL, Low density lipoprotein; PWV, Pulse wave velocity; SEARCH, for Diabetes in Youth Study; SES, Socio-economic status; TC, Total cholesterol; T1D, Type 1 Diabetes; T2D, Type 2 Diabetes; TG Triglycerides; WC, Waist Circumference; WHR, Waist to hip ratio.

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Aim: To test the hypothesis that intensive insulin treatment and optimal glycaemic control are not fully protective against reduction of insulin sensitivity in children

Material and methods: Cohort study of 78 normal-weight patients with prepubertal onset  $(T_0)$  and follow-up waves at 1  $(T_1)$ , 5  $(T_5)$ , 10  $(T_{10})$ , and 12  $(T_{12})$  years; matched for age and sex to 30 controls at  $T_{12}$ . Estimated insulin sensitivity (eIS) by three formulae; ultrasound evaluation of para and perirenal fat thickness; hepatic steatosis (HS); carotid intima media thickness (cIMT) at  $T_{12}$ .

Results: At T12, the 36 patients (46%) who had constantly or prevalently haemoglobin A1c (HbA1c) < 58 mmol/l during follow-up showed better eIS indexes (p = 0.049 to < 0.0001); lipid profile (p = 0.042 to < 0.0001), reduced fat mass (p = 0.012) and required lower insulin dose (p = 0.032) than the 42 patients (54%) with HbA1c  $\geq$  58 at T12. Patients (N = 25) with  $elS_{EDC} < 8.77 \text{ mg kg}^{-1} \text{ min}^{-1}$  showed higher cIMT (p < 0.0001). HS was found in 6 patients (~8%). In patients and normal-weight controls, fat mass (p = 0.03), age (p = 0.03), cIMT (p = 0.05) predicted HS; eIS indexes (p from 0.04 to < 0.0001)predicted cIMT. Body mass index, perirenal fat, fat mass, and triglycerides to high density lipoprotein cholesterol ratio were associated with eIS indexes (p from

**Conclusions:** Young T1D patients have reduced insulin sensitivity and higher cIMT. Adiposity, glucose, and lipid control over follow-up are likely to influence both. Enhanced adiposity seems of paramount relevance for the onset of HS in T1D patients alike in healthy youths.