UNIVERSITY OF CAMBRIDGE

Early detection and prevention of vascular complications in adolescents with type 1 diabetes

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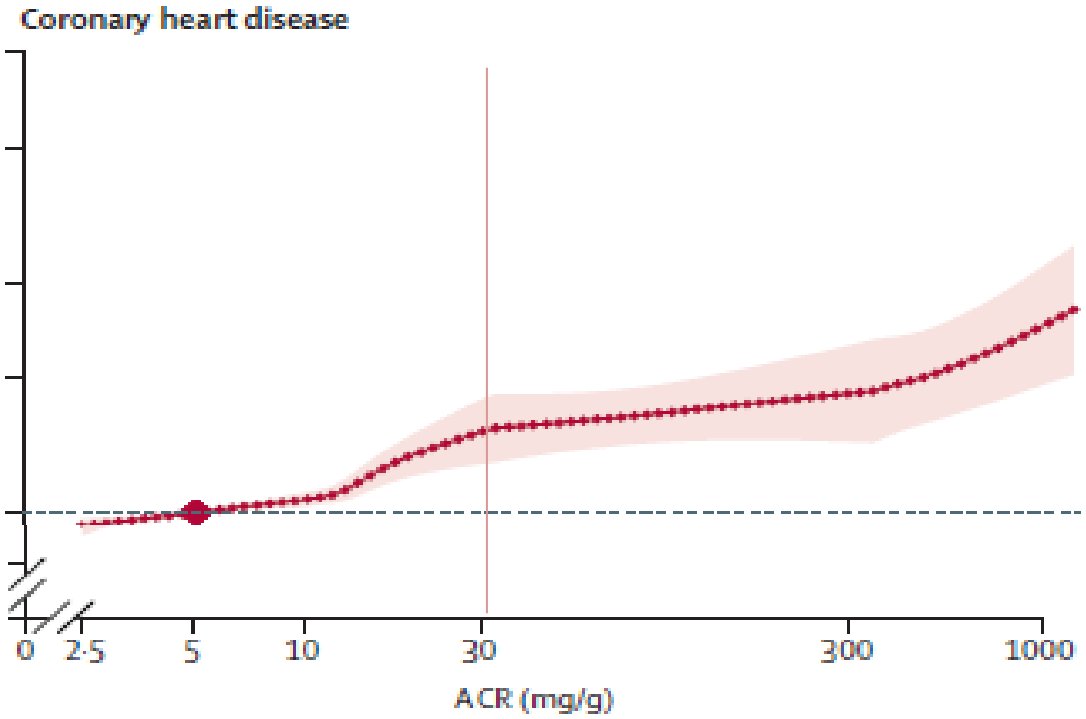
Diabetic kidney disease

- **Microvascular complications: 15-40%** patients with type 1 diabetes
- **Leading cause of End Stage Renal Disease (ESRD)**
- Maior determinant of **cardiovascular** morbiditv and mortalitv



Matsushita K et al, Lancet Diabetes Endocrinol 2015

Thomas MC et al, Nat Rev 2015

Aim of the study

- To assess whether early stratification based on tertiles of albumin-creatinine ratio (ACR) could identify adolescents with type 1 diabetes at higher risk of developing renal and cardiovascular complications.

Study population:

Adolescent Type 1 diabetes cardio-renal intervention Trial (AdDIT) cohort

- **840 Adolescents (age: 10-16 years) with T1D**
- **Normoalbuminuria** at baseline
- Screening: 3 early urine samples: **albumin-creatinine ratio (ACR)** and calculation of ACR tertiles

Low and Middle tertile ACR:
LOW-ACR group
n 400

Upper tertile ACR:
HIGH-ACR group
n 440

BASELINE AND FOLLOW UP ASSESSMENTS:

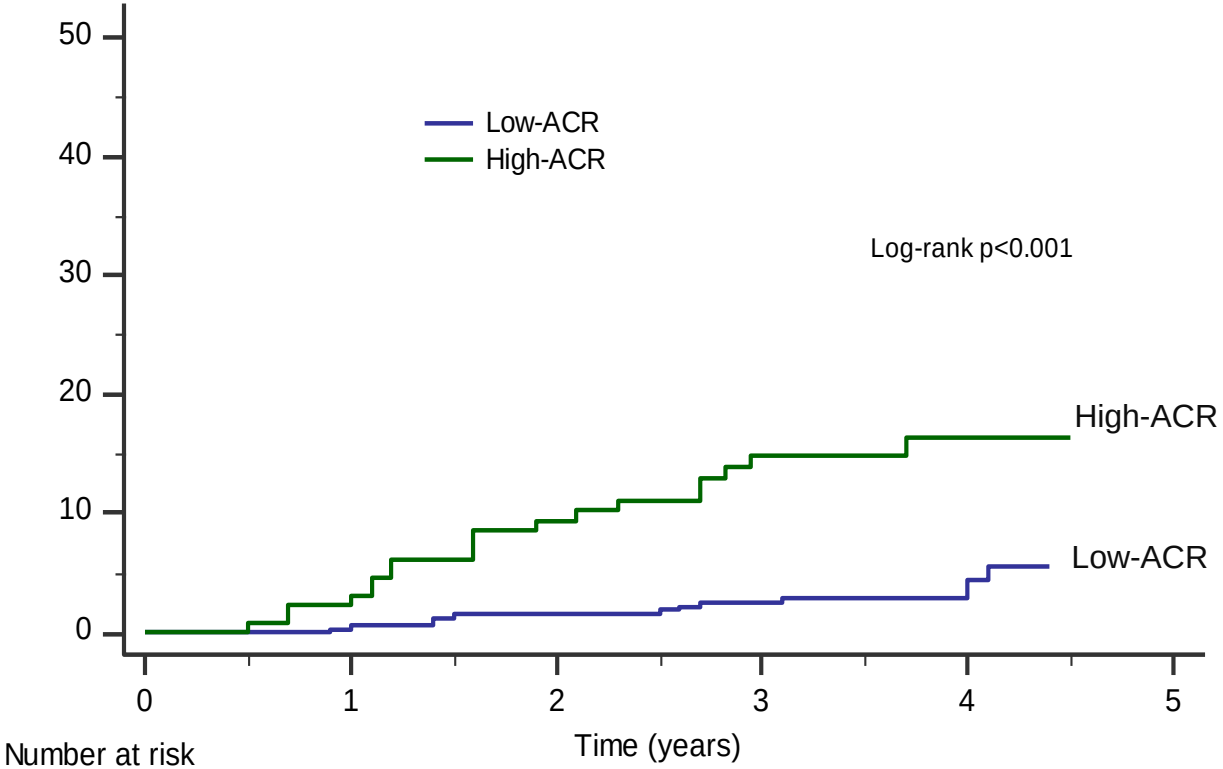
1. **Clinical data, HbA1c, Blood pressure**
2. **Renal markers:** ACR, eGFR
3. **Cardiovascular markers:** Lipid profile, High sensitivity C-reactive protein (hsCRP)
4. **Cardiovascular imaging:** carotid intima-media thickness (cIMT)

Baseline characteristics of the study population

	Low-ACR group	High-ACR group	p
N	400	150	
Sex (male, %)	211 (53.3)	77 (51.3)	0.95
Age (yr)	14.3 (1.6)	14.1 (1.6)	0.17
T1D Duration (yr)	7.3 (3.4)	5.9 (3.1)	<0.001
BMI (Kg/m^2)	21.9 (3.8)	21.6 (3.6)	0.38
HbA1c (mmol/mol)	68.8 (14.2)	69.3 (14.6)	0.72
Systolic blood pressure (mmHg)	115.6 (11.3)	116.4 (13.3)	0.52
Diastolic blood pressure (mmHg)	67.1 (7.7)	65.6 (7.8)	0.05
HDL Cholesterol (mmol/l)	1.5 (0.4)	1.6 (0.4)	0.71
LDL Cholesterol (mmol/l)	2.4 (0.7)	2.3 (0.7)	0.62
hsC-reactive protein (mg/l)	0.49 (0.19; 1.14)	0.59 (0.19; 1.20)	0.21
eGFR (ml/min/1.73m^2)	128.5 (21.2)	135.2 (24.6)	0.007

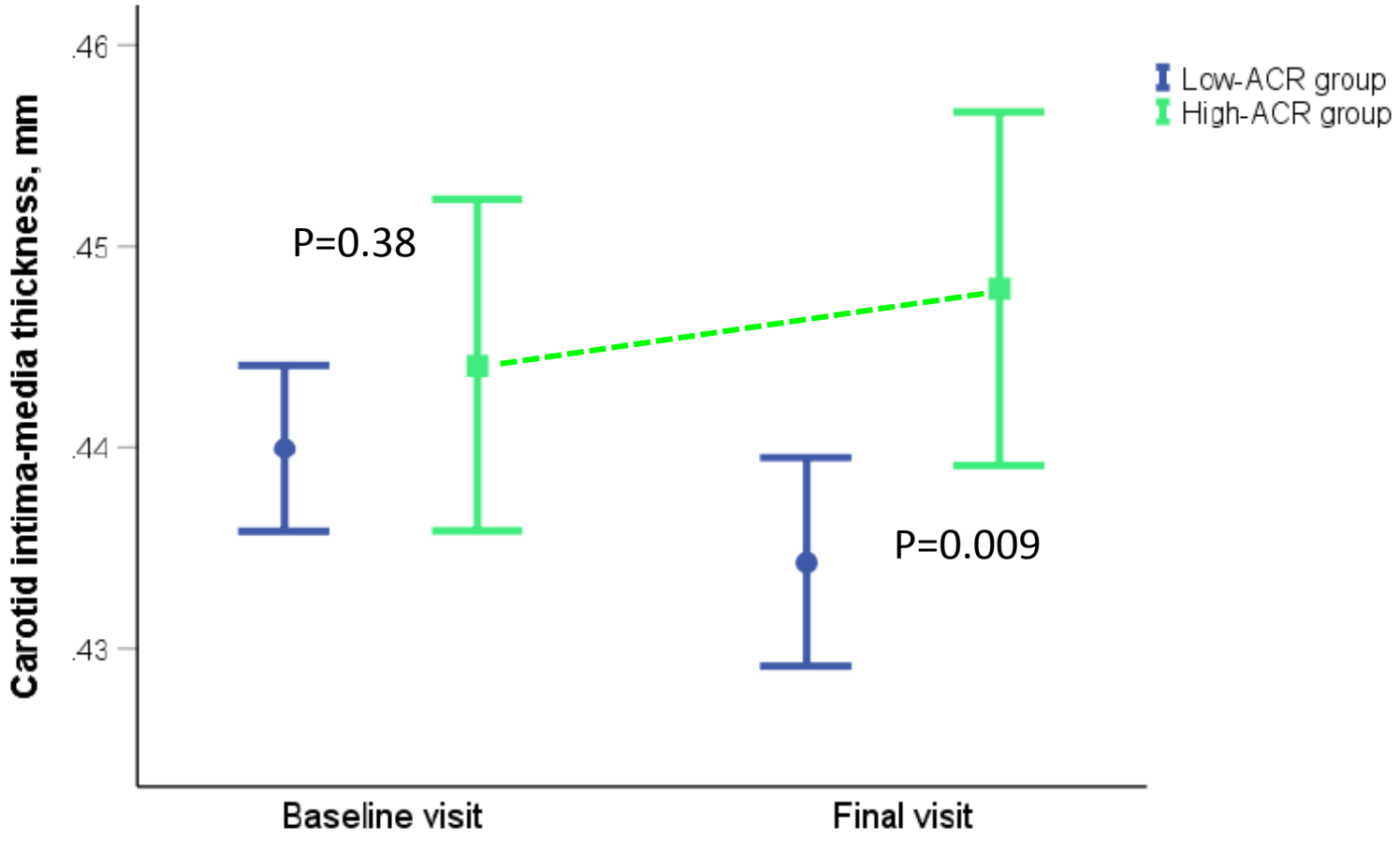
Data are mean (SD) or median (IQR)

Primary endpoint:
Cumulative Incidence of microalbuminuria in relation to baseline ACR



	HR	95% CI
ACR category	4.52	2.20; 9.33
HbA1c, per %	1.39	1.11; 1.73

Secondary endpoint:
Changes in Carotid intima-media thickness in relation to baseline ACR



Data are means and 95% CI

Other secondary endpoints: Changes in cardiovascular and renal markers in relation to baseline ACR

	β-Estimate (SE)	P
Systolic blood pressure (mmHg)	2.08 (1.00)	0.01
Diastolic blood pressure (mmHg)	-0.06 (0.58)	0.92
Total cholesterol (mmol/l)	-0.11 (0.09)	0.20
HDL cholesterol (mmol/l)	-0.05 (9.04	0.11
LDL cholesterol (mmol/l)	-0.08 (0.07)	0.29
Triglycerides (mmol/l)	0.08 (0.06)	0.10
hs C-Reactive Protein (mg/dl)	0.85 (0.32)	0.008
eGFR (ml/min/1.73m²)	4.84 (1.49)	0.01

Data are from linear mixed models and reported as β-Estimate and standard error (SE)

Summary and Conclusions

- A higher ACR even within the normal range was associated with:
  - a greater risk of progression to microalbuminuria
  - a worse cardiovascular profile: greater cIMT, blood pressure and hsCRP values

- Early screening for abnormal ACR may provide a valuable tool to identify adolescents at high risk for vascular complications

- Selection of high-risk groups based on urinary albumin excretion may improve the precision of adolescent interventions.