Background
- Experimental and clinical studies have suggested that insulin resistance, or its in vivo compensatory equivalent, hyperinsulinaemia, may initiate or sustain cardiovascular disease.
- However, there is currently no evidence for a direct relationship between insulin resistance and atherosclerosis or cardiovascular disease. Previous studies have used surrogate markers of insulin resistance in cohorts of subjects with multiple risk factors.

Objectives
- To test whether there is a direct link between insulin resistance and atherosclerosis in a low-risk Caucasian population.
- To establish whether the development of early atherosclerotic changes over time is accelerated in insulin-resistant healthy subjects.

Design

Relationship Between Insulin Sensitivity and Cardiovascular Disease Risk (RISC) Study
- Relation of insulin sensitivity to intima-media thickness (IMT) of carotid arteries, a surrogate marker of systemic atherosclerotic load, at baseline and after 3-years of follow-up.
- In this report, baseline, cross-sectional data are presented.
- Over 1500 subjects were recruited at 19 centres in 14 European countries and are being followed-up.

Study Population
- 1569 subjects recruited.
  - Inclusion criteria:
    - 2-hour glucose <11.1 mmol/L
    - SBP <140/<90 mmHg
  - Exclusions:
    - Cardiovascular disease, chronic illness, significant smokers
    - M value (µmol.min⁻¹.kgf⁻²)
    - 2-hour insulin (pmol/L)
    - IMT (m)

Baseline Examinations
- Lifestyle and medical history questionnaire.
- Anthropometry.
- Biological samples + oral glucose tolerance test.
- Euglycaemic hyperinsulinaemic clamp.
- Ultrasound (US) examination of extracranial carotid arteries.

B-mode US of Carotid Arteries
- IMT of the near and far arterial wall was measured off-line in digitised images at the level of common carotid artery.
- The overall average IMT of all segments was also calculated: IMT Total

Characteristics of Study Population
- 146 subjects satisfying inclusion criteria.

Main Determinants of IMT Total

Associations between IMT and 2-hour glucose or M value were statistically significant but weak and were lost after adjustment for the main determinants of IMT.

Conclusions
- In cross-sectional observations in a low-risk population, insulin resistance is not an independent predictor of carotid artery IMT.
- The follow-up phase of the RISC Study will conclusively test whether insulin resistance per se is atherogenic.

*Acknowledgements
- EUGIR-RISC Study Group

Further information on the RISC project and participating centres can be found at www.risc.org.

Presented at the 41st EASD Annual Meeting Athens, Greece 10-15 September 2005.