Diabetes journals

DIABETES

AST and ALT linked with risk of incident type 2 diabetes

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

1 Few studies have reported associations of markers of liver injury, including elevated concentrations of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), with prospective risk of type 2 diabetes.

2 The purpose of this study was to investigate the associations of elevated AST and ALT with incident type 2 diabetes among 906 participants in the Insulin Resistance Atherosclerosis Study who were non-diabetic at baseline.

3 Insulin sensitivity and acute insulin response were measured directly from the frequently sampled intravenous glucose tolerance test among black, Hispanic and non-Hispanic white participants aged 40–69 years.

4 After 5.2 years, 148 people had developed type 2 diabetes. Baseline AST and ALT were positively correlated with fasting insulin, waist circumference and fasting glucose, and inversely with insulin sensitivity.

5 When entered into the same model with adjustment for demographic variables, both C-reactive protein and ALT independently predicted type 2 diabetes.

6 In addition, AST and ALT were positively associated with incident type 2 diabetes after excluding former and moderate-to-heavy drinkers.

7 In conclusion, AST and ALT independently predict type 2 diabetes. Baseline elevations of these markers may reflect non-alcoholic fatty liver disease or related pathologies.

Hanley AJG, Williams K, Festa A et al (2004) Elevations in markers of liver injury and risk of type 2 diabetes. Diabetes **53**: 2623–32

Elevated markers of liver injury can predict diabetes

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Elevated levels of aspartate aminotransferase (AST) and alaninamino-transferase (ALT), as markers of liver injury, have been reported to be associated with prospective risk of type 2 diabetes. However, previous studies have not adjusted for insulin sensitivity, which has an important association with obesity and non-alcoholic fatty liver disease.

This paper investigated the associations of elevated AST and ALT with incidence of type 2 diabetes in the Insulin Resistance Atherosclerosis Study, in patients who did not have diabetes at baseline. Insulin sensitivity and acute insulin response were measured directly from the frequently sampled intravenous glucose tolerance test among black, Hispanic and non-Hispanic Caucasian participants aged 40–69 years.

Of 906 participants, 148 developed type 2 diabetes after 5.2 years. Baseline AST and ALT were positively correlated with fasting insulin, waist circumference and fasting glucose levels, which were all inversely correlated with insulin sensitivity. Adjusting for age, sex, ethnicity and alcohol consumption still revealed those with the highest AST and ALT levels to be at significantly increased risk of incident type 2 diabetes, compared with those of lower values of AST and ALT. After a further adjustment for smoking, waist circumference, triglyceride, high-density lipoprotein, impaired glucose tolerance, insulin sensitivity and acute insulin response, both AST and ALT remain significantly associated with incident type 2 diabetes. Further logistic regression analysis demonstrated that both C-reactive protein and ALT independently predicted type 2 diabetes.

Thus, AST and ALT independently predict type 2 diabetes. Baseline elevations of these markers may reflect non-alcoholic fatty liver disease.

DIABETOLOGIA

Moderate alcohol intake lowers markers of inflammation

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 Type 2 diabetes is characterised by heightened inflammation and endothelial dysfunction. Moderate alcohol intake has been associated with a reduced risk of cardiovascular disease in patients with type 2 diabetes.

2 This article investigated the relationship between alcohol intake and inflammation in 726 of 18 159 men who returned blood samples in the Health Professionals Follow-up Study and had confirmed type 2 diabetes at baseline.

3 In age-adjusted analyses, alcohol intake was associated with higher levels of high-density lipoprotein (HDL) cholesterol and adiponectin and lower levels of HbA_{1c}, soluble tumour necrosis factor receptor-2 (sTNF-R2), fibrinogen and soluble vascular adhesion molecule-1 (sVCAM-1).

4 Each additional drink per day was related to increased HDL cholesterol and adiponectin, and decreased fibrinogen, sTNFR-2 and sVCAM-1 after adjusting for HbA_{1c}, insulin use, fasting status, body mass index, physical activity, smoking, prevalence of cardiovascular disease, aspirin use, and dietary factors.

5 When patients were stratified according to HbA_{1c} levels, the relationship between alcohol and inflammatory biomarkers persisted.

6 In people with type 2 diabetes, moderate alcohol intake may have a beneficial effect on markers of inflammation and endothelial dysfunction.

Shai I, Rimm EB, Schulze MB, Rifai N, Stampfer MJ, Hu FB (2004) Moderate alcohol intake and markers of inflammation and endothelial dysfunction among diabetic men. Diabetologia **47**: 1760–67

'The authors designed an experimental paradigm in vitro that mimics the main defect of insulin resistance, namely a blockade of the phosphatidyl-inositol (PI) 3-kinase-dependent pathway.'

'...treatment of insulin-resistant individuals must include effective measures to reduce insulin resistance (i.e. to improve insulin sensitivity) and to decrease insulinaemia.'

DIABETES

Insulin resistance blocks PI 3-kinase signalling pathway

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓✓

1 Insulin resistance is concomitant with type 2 diabetes, hypertension, obesity and other features of the metabolic syndrome. The individual contributions of insulin resistance and associated compensatory hyperinsulinaemia remain incompletely understood.

2 The authors designed an experimental paradigm in vitro that mimics the main defect of insulin resistance, namely a blockade of the phosphatidylinositol (PI) 3-kinase-dependent pathway.

3 Under normal circumstances, insulin exerts its antiatherogenic action in endothelial cells and vascular smooth muscle cells (VSMCs) via the PI 3-kinase signalling pathway. Antiatherogenic aspects of insulin action include stimulation of nitric oxide production, counteraction of VEGF and PDGF effects, and maintenance of a differentiated state of VSMCs.

4 In the presence of metabolic insulin resistance (i.e. diminished strength of the PI 3-kinase signalling), the resulting compensatory hyperinsulinaemia becomes proatherogenic, stimulating both the mitogen-activated protein-kinase signalling pathway and excessive prenylation of Ras and Rho proteins.

5 Therefore, treatment of insulin-resistant individuals must include effective measures to reduce insulin resistance (i.e. to improve insulin sensitivity) and to decrease insulinaemia.

Low Wang CC, Goalstone ML, Draznin B (2004) Molecular mechanisms of insulin resistance that impact cardiovascular biology. Diabetes **53:** 2735–40

DIABETOLOGIA

Insulin resistance increases CHD risk

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓✓

1 The study examined men with diabetes or coronary heart disease (CHD) or both for markers of haemostasis and inflammation, and assessed the relationship between these markers and insulin resistance in men with type 2 diabetes; 426 men had prevalent type 2 diabetes and 842 had prevalent CHD.

2 Irrespective of CHD status, men with type 2 diabetes were more likely to have multiple risk factors and higher levels of haemostatic and inflammatory markers compared to men without.

3 In men with type 2 diabetes, increased insulin resistance is associated with increased prevalence of CHD and of activated haemostasis and dyslipidaemia.

4 The tendency of men with diabetes to develop thrombosis and hence CHD risk may be reduced by reducing insulin resistance.

Wannamethee SG, Lowe GDO Shaper AG et al (2004) Insulin resistance, haemostatic and inflammatory markers and coronary heart disease risk factors in type 2 diabetic men with and without coronary heart disease. Diabetologia **47**: 1557–65

DIABETES RESEARCH AND CLINICAL PRACTICE

baPWV is linked with CV risk factors of metabolic syndrome

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 The authors studied the association between brachial-ankle pulse wave velocity (baPWV), a non-invasive means of measuring atherosclerosis, and metabolic syndrome cardiovascular (CV) risk factors.

2 Anthropometric parameters, fasting blood glucose, blood pressure, lipid profiles, baPWV and ankle-brachial pressure index were measured in 368 people without history of diabetes or hypertension.

3 In women, baPWV was closely associated with the CV risk factors of the metabolic syndrome. Women without the metabolic syndrome showed lower baPWV levels compared to women with the metabolic syndrome.

Choi KM, Lee KW, Seo JA et al (2004) Relationship between brachial-ankle pulse wave velocity and cardiovascular risk factors of the metabolic syndrome. Diabetes Research and Clinical Practice **66**: 57–61

DIABETES

Elevated ALT levels predict incident type 2 diabetes

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

1 The study examined the association between serum alanine aminotransferase (ALT) and features of the metabolic syndrome in 5974 men. It also examined whether ALT predicted incident diabetes independently of routinely measured factors.

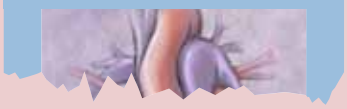
2 During 4.9 years follow up, a total of 139 men developed new diabetes. ALT levels increased progressively with the increasing number of metabolic syndrome abnormalities.

3 Men with ALT ≥29 units/l had an elevated risk for diabetes versus those with ALT <17 units/l.

4 Thus, elevated ALT levels predict incident diabetes. ALT enzyme activity could be included in future diabetes prediction algorithms as it is simple to measure and tests can be carried out in routine clinical practice.

Sattar N, Scherbakova O, Ford I et al (2004) Elevated alanine aminotransferase predicts new-onset type 2 diabetes independently of classical risk factors, metabolic syndrome and C-reactive protein in the West of Scotland Coronary Prevention Study. Diabetes **53**: 2855–60

DIABETOLOGIA



Spironolactone impairs heart rate variability

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The authors postulated that aldosterone blockade with spironolactone might have beneficial effects on the prognostic markers of endothelial function and heart rate variability in patients with diabetes.

2 In this randomised, double-blind trial, 42 patients had their endothelial function assessed by forearm venous occlusion plethysmography after one month of spironolactone treatment or placebo. Twenty of the 42 participants were on angiotensin-converting enzyme (ACE) inhibitor therapy. At the end of each treatment period, heart rate variability, HbA_{1c} and plasma angiotensin II levels were assessed.

3 The group on spironolactone had a decrease in forearm blood flow response to acetylcholine of 44.56±14.56 % (p=0.003) compared to placebo, and a decrease of 57.61±15.56 % (p<0.001) in the 20 patients on ACE inhibition.

4 Spironolactone also worsened heart rate variability parameters. HbA_{1c} and angiotensin II increased during treatment with spironolactone by 0.26±0.07 % (p=0.001) and 8.12±1.94 μg/ml (p=0.001) respectively.

5 Endothelial function and heart rate variability were worsened in patients with type 2 diabetes on spironolactone. Worsening glycaemic control and increase in plasma angiotensin II seen with spironolactone treatment may have resulted in these findings.

6 Thus the prescribing of spironolactone to patients with diabetes without heart failure does not seem to be justified.

Davies JI, Band M, Morris A, Struthers AD (2004) Spironolactone impairs endothelial function and heart rate variability in patients with type 2 diabetes. Diabetologia **47**: 1687–94

DIABETES RESEARCH AND CLINICAL PRACTICE

Candesartan reduces proteinuria

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 This multi-centre, randomised, double-blind study examined the effect of candesartan cilexetil, an angiotensin II receptor blocker, on proteinuria in Japanese people with type 2 diabetes.

2 Patients with diabetes and confirmed proteinuria were enrolled into four groups for 12 weeks' treatment with candesartan cilexetil 2, 4 or 8 mg or placebo. The contribution of the angiotensin-converting enzyme (ACE) gene polymorphism to the effect of candesartan cilexetil was also examined.

3 After 12 weeks of treatment, candesartan cilexetil showed a dose-related reduction in proteinuria in 127 patients, with a 18.1% reduction in the 4 mg group and a 5.8 % reduction in the 8 mg group. This contrasted with a 0.8 % increase in the 2 mg group and a 32.2 % increase in the placebo group.

4 There was no correlation between blood pressure and proteinuria, and the dose-response effect of candesartan cilexetil on proteinuria remained significant even after adjusting for mean blood pressure.

5 These results clearly indicate that the antiproteinuric effects of candesartan cilexetil are independent of its general antihypertensive action.

Haneda M, Kikkawa R, Sakai H, Kawamori R for Candesartan in Diabetic Nephropathy Study Group (2004) Antiproteinuric effect of candesartan cilexetil in Japanese subjects with type 2 diabetes and nephropathy. Diabetes Research and Clinical Practice **66**: 87–95

DIABETES

Lower lipid levels reduce risk of macular oedema

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓✓

1 This study of people with type 1 diabetes examined the relationship between serum lipid levels and clinically significant macular oedema, hard exudates and other diabetic retinopathy (DR) end points.

2 Data were studied from annually measured serum lipids among the 1441 participants in the Diabetes Control and Complications Trial.

3 The relationship of the cumulative average of lipid levels with the development of clinically significant macular oedema, hard exudate, DR progression and development of proliferative DRP were examined using proportional hazards regression models.

4 Total-to-high-density lipoprotein cholesterol ratio and low-density lipoprotein predicted the development of clinically significant macular oedema and hard exudate in models controlling for primary prevention vs secondary intervention subgroup, HbA_{1c}, randomised treatment assignment and other risk factors.

5 After adjustment for HbA_{1c}, relationships of lipids with the progression of DR and development of proliferative DR were weaker and not significant.

6 An increased risk of clinically significant macular oedema and retinal hard exudate is associated with higher serum levels. Risk of clinically significant macular oedema, an important cause of vision loss in patients with type 1 diabetes, may be reduced by the use of lipid-lowering treatment.

Miljanovic B, Glynn RJ, Nathan DM, Manson JE, Schaumberg DA (2004) A prospective study of serum lipids and risk of diabetic macular edema in type 1 diabetes. Diabetes **53**: 2883–92

'This study examined the relationship between serum lipid levels and clinically significant macular oedema, hard exudates and other diabetic retinopathy (DR) endpoints in a population with type 1 diabetes.'

'Lipid-lowering treatment among patients with type 1 diabetes, recommended to prevent cardiovascular disease, may also decrease risk of clinically significant macular oedema, an important cause of vision loss.'