Diabetes journals

DIABETES CARE

Rosiglitazone improves insulin sensitivity

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

1 The aim of this study was to test whether vascular reactivity is modified by improving metabolic control and peripheral insulin resistance in patients with type 2 diabetes.

2 In a randomised, double-blind design, 74 patients with type 2 diabetes were assigned to rosiglitazone (8 mg/day), metformin (1500 mg/day) or placebo for 16 weeks.

3 Insulin sensitivity (euglycaemic insulin clamp), ambulatory blood pressure and forearm blood flow response to intra-arterial acetylcholine (ACh), intra-arterial nitroprusside, the clamp and blockade of nitric oxide (NO) synthase were determined.

4 Patients had reduced insulin sensitivity and reduced maximal response to ACh. Relative to placebo, 16 weeks of rosiglitazone and metformin similarly reduced fasting glucose and HbA_{1c}. Insulin sensitivity increased with rosiglitazone but not with metformin or placebo.

5 Ambulatory diastolic blood pressure fell consistently only in the rosiglitazone group. Nitroprusside dose response, clamp-induced vasodilatation and NO blockade were not affected by either treatment. In contrast, the slope of the ACh dose response improved with rosiglitazone, but did not change with either metformin or placebo.

6 At equivalent glycaemic control rosiglitazone, but not metformin, improves endothelium-dependent vasodilatation and insulin sensitivity in patients with type 2 diabetes.

Natali A, Baldeweg S, Toschi E et al (2004) Vascular effects of improving metabolic control with metformin or rosiglitazone in type 2 diabetes. *Diabetes Care* **27**: 1349–57

Encouraging anti-atherosclerotic effect of rosiglitazone

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It is now well established that a key early event in the development of atherosclerosis is endothelial dysfunction, a characteristic feature of which is a reduction in the bioactivity of the signalling reactive nitrogen intermediate, nitric oxide (NO). Reduced NO bioactivity can be as a result of reduced production of NO or increased inactivation by reactive oxygen species. NO is thought to be an anti-atherosclerotic molecule, with properties including vasodilatation, inhibition of vascular smooth muscle growth, leukocyte adhesion and platelet adherence and aggregation. Recent studies in support of this have shown that endothelial dysfunction assessed using vasodilatation to acetylcholine in different vascular territories is predictive of future cardiovascular events.

Type 2 diabetes is characterised by significant endothelial dysfunction and accelerated atherosclerosis. Exploring the effect of different therapies on endothelial function in people with diabetes is therefore of particular importance.

In this elegant study, Natali et al (2004) compared the effect of administering the insulin-sensitising agents metformin and rosiglitazone (at doses leading to similar glucose reductions) for 16 weeks on acetylcholine and insulin-mediated increases in forearm blood flow, ambulatory blood pressure, glucose homeostasis and circulating cytokines. The study showed that, compared with placebo, rosiglitazone but not metformin improves insulin sensitivity and endothelial function and also leads to a modest but significant decline in blood pressure. Rosiglitazone therapy was also associated with a tendency for circulating cytokines to fall.

Of all disorders predisposing to atherosclerosis, type 2 diabetes is possibly associated with the worst endothelial function. This is probably a result of the endothelium being exposed to a collection of vascular risk factors, including hypertension, abnormal lipids, inflammatory cytokines, C-reactive protein and hyperglycaemia. The results of the study by Natali et al provide encouraging data supporting a potential anti-atherosclerotic effect of the thiazolidinediones. Moreover, the study also shows that in order to 'tone-up' endothelial function in patients with type 2 diabetes, a multi-factorial approach is necessary.

DIABETES CARE

High incidence of CHF in patients with type 2 diabetes

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

1 In order to update previous estimates of the congestive heart failure (CHF) incidence rate in patients with type 2 diabetes and describe its risk factors, 8231 patients with type 2 diabetes and 8845 patients of similar age and sex who did not have diabetes or CHF were followed up for six years.

2 Patients with diabetes were much more likely to develop CHF than patients without diabetes. The difference in CHF development rates between people with and without diabetes was much greater in younger age groups.

3 In addition to age and ischaemic heart disease, poorer glycaemic control and greater body mass index were important predictors of CHF development.

4 The CHF incidence rate in type 2 diabetes is 3–15 times greater than the previously reported; 2–10 cases per 1000 patients.

5 Multivariate results emphasise the importance of controlling modifiable risk factors for CHF, such as hyperglycaemia, elevated blood pressure and obesity. Younger patients may benefit most from risk factor modification.

Nichols GA, Gullion CM, Koro CE et al (2004) The incidence of congestive heart failure in type 2 diabetes. *Diabetes Care* **27**: 1879–84

'The Detection of Ischaemia in Asymptomatic Diabetics study was designed to determine the prevalence and severity of inducible myocardial ischaemia in asymptomatic patients with type 2 diabetes.'

'Silent myocardial ischaemia occurs in greater than one in five asymptomatic patients with type 2 diabetes.'

DIABETES CARE

Silent myocardial ischaemia detected in asymptomatic patients

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

1 The Detection of Ischaemia in Asymptomatic Diabetics study was designed to determine the prevalence and severity of inducible myocardial ischaemia in asymptomatic patients with type 2 diabetes.

2 In this study, 1123 patients with type 2 diabetes aged 50–75 years with no known or suspected coronary artery disease were randomly assigned to either stress testing and five-year clinical follow up, or to follow up only. The prevalence of ischaemia in 522 patients randomised to stress testing was assessed using adenosine-stress single photon emission-computed photography myocardial perfusion imaging.

3 A total of 113 patients (22 %) had silent ischaemia, including 83 with regional myocardial perfusion abnormalities and 30 with normal perfusion but other abnormalities. Moderate or large perfusion defects were present in 33 patients.

4 The strongest predictors for abnormal tests were abnormal Valsalva and diabetes duration; other cardiac risk factors or inflammatory and prothrombotic markers were not predictive. Adenosine-induced ST depression was more common in women.

5 Silent myocardial ischaemia occurs in greater than one in five asymptomatic patients with type 2 diabetes. Traditional and emerging cardiac risk factors were not associated with an abnormal stress test, although cardiac autonomic dysfunction was a strong predictor of ischaemia.

Wackers FJT, Young LH, Inzucchi SE et al (2004) Detection of silent myocardial ischaemia in asymptomatic diabetic subjects. *Diabetes Care* **27**: 1954–61

DIABETES CARE

Lowering the FPG criterion increases prevalence of IFG

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

1 The study's aims were to determine the effect of lowering the fasting plasma glucose (FPG) criterion for impaired fasting glucose (IFG) on the prevalence of IFG, and the risks of diabetes and cardiovascular disease (CVD) associated with IFG.

2 Data from three large studies were used. Lowering the criterion for diagnosing IFG to 5.6 mmol/l increased the prevalence of IFG from 9.5 to 32.3%. The lower cut-off identified more patients at risk of diabetes and ischaemic heart disease, but the relative risk was lower than that for IGT.

3 Greater efforts to identify those with IGT, or a group at similar risk of diabetes and CVD, may be a more efficient public health measure than lowering the FPG criterion for diagnosing IFG.

Tai ES, Goh SY, Lee JJM et al (2004) Lowering the criterion for impaired fasting glucose. *Diabetes Care* **27**: 1728–34

DIABETOLOGIA

Hyperinsulinaemia associated with CV mortality

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

1 The association between plasma insulin and cardiovascular (CV) mortality in 6156 men and 5351 women without diabetes (aged 30–89 years) was examined using data from 11 prospective studies.

2 During the 8.8-year follow up, 362 men and 70 women died from CV disease. The age- and smoking-adjusted overall hazard ratio of CV mortality was 1.58 in men and 2.64 in women. For 2-hour plasma insulin, these hazard ratios were 1.28 and 1.36, respectively.

3 Hyperinsulinaemia, defined by the highest quartile cut-off for fasting insulin, was significantly associated with CV mortality in both men and women independently of other risk factors.

The DECODE Insulin Study Group (2004) Plasma insulin and cardiovascular mortality in non-diabetic European men and women: a meta-analysis of data from eleven prospective studies. *Diabetologia* **47**: 1245–56

DIABETOLOGIA

Risk factor status more adverse in diabetes

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

1 The authors examined risk factor management in patients with and without diabetes who have coronary heart disease (CHD), based on 3569 patients from the EUROASPIRE I survey and 5556 patients from the EUROASPIRE II study.

2 In EUROASPIRE I and II, 18 % and 20 % of patients with CHD respectively had been previously diagnosed with diabetes.

3 In EUROASPIRE II the prevalence of risk factors (known diabetes/no diabetes) was: current smoking (17 %/22 %); obesity (43 %/29 %); raised blood pressure (57 %/49 %); and elevated total cholesterol (55 %/59 %).

4 These European surveys show a high prevalence of adverse lifestyles and modifiable risk factors among patients with and without diabetes who have CHD. The risk factor status was more adverse in patients with diabetes.

Pyorala K, Lehto S, DeBacquer D et al (2004) Risk factor management in diabetic and non-diabetic patients with coronary heart disease. *Diabetologia* **47**: 1257–65

DIABETOLOGIA

Vitamin E has a beneficial effect on endothelial function

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

1 The impact of early vitamin E supplementation on vascular function in diabetes remains unresolved. Therefore, the authors examined the effects of vitamin E on functional and structural parameters and on chemical markers that are disturbed in diabetes in mesenteric and femoral arteries.

2 Segments of both arteries, taken from control and eight-week-old Wistar rats with streptozotocin-induced diabetes who were either treated with vitamin E or not, were mounted and assessed for endothelium-dependent and -independent vasodilation.

3 Early vitamin E supplementation has a beneficial effect on diabetes-induced endothelial dysfunction in resistant arteries.

Wigg SJ, Tare M, Forbes J et al (2004) Early vitamin E supplementation attenuates diabetes-associated vascular dysfunction and the rise in protein kinase C-β in mesenteric artery and ameliorates wall stiffness in femoral artery of Wistar rats. *Diabetologia* **47**: 1038–46

DIABETES CARE

Adiponectin linked with better glycaemic control

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

1 Adiponectin appears to play an important role in hyperglycaemia and dyslipidaemia as well as in inflammatory mechanisms, which lead to a markedly increased atherosclerotic risk in patients with diabetes.

2 Blood samples were taken from 741 men with type 2 diabetes who were in the Health Professionals Follow Up Study. Plasma levels of adiponectin and HbA_{1c}, blood lipids and inflammatory markers were examined.

3 Plasma adiponectin levels were positively correlated with high-density-lipid (HDL) cholesterol and negatively correlated with triglycerides, apolipoprotein B-100, C-reactive protein and fibrinogen. Associations between adiponectin and inflammatory markers were independent of HbA_{1c} and HDL cholesterol.

4 The study supports the hypothesis that increased adiponectin levels might be associated with better glycaemic control, better lipid profile and reduced inflammation in patients with diabetes.

Schulze MB, Rimm EB, Shai I, Rifai N, Hu FB (2004) Relationship between adiponectin and glycaemic control, blood lipids and inflammatory markers in men with type 2 diabetes. *Diabetes Care* **27**: 1680–87

DIABETES CARE

Ragaglitazar gives glycaemic control

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

1 Ragaglitazar improves plasma glucose and lipid profiles. The aim of the dose-ranging study was to assess the efficacy and safety of ragaglitazar in patients with type 2 diabetes.

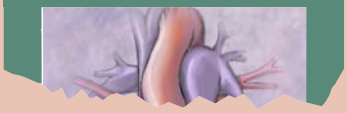
2 The study included 177 patients with type 2 diabetes with elevated levels of triglycerides, who received ragaglitazar, placebo or pioglitazone.

3 Ragaglitazar 0.1 mg was similar to placebo, whereas a maximal hypoglycaemic effect was seen at 4 mg.

4 Ragaglitazar provided glycaemic control that was comparable with that of pioglitazone and, compared with placebo, provided significant improvement in the lipid profile.

Saad MF, Greco S, Osei K et al (2004) Ragaglitazar improves glycaemic control and lipid profile in type 2 diabetic subjects. *Diabetes Care* **27**: 1324–29

DIABETES CARE



ACE inhibitors reduce CV-related mortality

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

1 Angiotensin-converting enzyme (ACE) inhibitor therapy is widely used in lower-risk patients with type 2 diabetes to reduce mortality, despite limited evidence.

2 The aim of this study was to evaluate the association between ACE inhibitor use and mortality in patients with diabetes and no cardiovascular (CV) disease.

3 The analysis included 6176 patients: 1187 patients in the ACE inhibitor cohort and 4989 in the control group. Subjects were prospectively followed until death or the end of 1999. Multivariate Cox proportional hazards models were used to assess differences in all-cause and CV-related mortality between cohort groups.

4 Patients were 60.7 +/- 13.7 years old, 43.6 % female, and were followed for an average of 5.3 +/- 2.1 years. Mean duration of ACE inhibitor therapy was 3.6 +/- 1.8 years.

5 There were significantly fewer deaths in the ACE inhibitor group (102; 8.6 %) compared with the control cohort (853; 17.1%), with an adjusted hazard ratio (HR) and 95 % confidence interval of 0.49 (0.40–0.61) ($p<0.001$). CV-related mortality was also reduced (40 (3.4 %) *vs* 261 (5.2 %); adjusted HR 0.63 (0.44–0.90); $p=0.012$).

6 The use of ACE inhibitors was associated with a significant reduction in all-cause and CV-related mortality in a broad spectrum of patients with type 2 diabetes and no CV disease.

Eurich DT, Majumdar SR, Tsuyuki RT, Johnson JA (2004) Reduced mortality associated with the use of ACE inhibitors in patients with type 2 diabetes. *Diabetes Care* **27**: 1330–34

'The aim of this study was to evaluate the association between ACE inhibitor use and mortality in patients with diabetes and no cardiovascular (CV) disease.'

'The use of ACE inhibitors was associated with a significant reduction in all-cause and CV-related mortality in a broad spectrum of patients with type 2 diabetes and no CV disease.'