

Cardiovascular disease & diabetes

Should clopidogrel be the antiplatelet agent of choice in people with diabetes?



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Patients with diabetes are at high risk of recurrent vascular events. Aspirin is frequently used to reduce recurrence because it is an inexpensive intervention, but other than its use in patients with acute coronary syndromes the benefits are relatively modest.

Clopidogrel is a newer, more expensive antiplatelet agent that is indicated for use in preventing vascular events in patients with a history of symptomatic atherosclerotic disease, and in patients with unstable angina. The study by Bhatt et al (below) provides the evidence base for the prevention of vascular events in patients with diabetes and a history of symptomatic atherosclerotic disease.

The CAPRIE trial (Clopidogrel versus Aspirin in Patients at Risk of Ischaemic

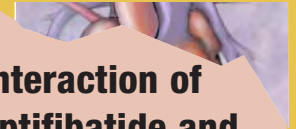
Events) compared the efficacy of clopidogrel 75 mg versus aspirin 325 mg in more than 19 000 patients. The primary end-point was a combination of ischaemic stroke, myocardial infarction, or vascular death, and clopidogrel was slightly, but significantly, more effective than aspirin.

Nearly 4000 of the subjects had a previous history of diabetes, and Bhatt's paper describes a post-hoc, subgroup analysis using an extended end-point of vascular death, myocardial infarction, all-cause stroke and re-hospitalisation for ischaemic events. No justification is given for the extended end-point.

Again, clopidogrel was more effective than aspirin in reducing events in this very high-risk group of patients. Has the time come to make clopidogrel the antiplatelet agent of choice in people with diabetes?

A randomised, blinded trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE) (1996) *The Lancet* **348**: 1329–39

AMERICAN JOURNAL OF CARDIOLOGY



Interaction of eptifibatide and diabetes after stenting

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

- Blockade of the glycoprotein IIb/IIIa receptor with eptifibatide following coronary artery stenting reduces the incidence of ischaemic complications.
- The interaction of eptifibatide with diabetes in patients undergoing coronary artery stenting was evaluated in this study by analysing 1-year outcomes of 466 diabetic and 1595 non-diabetic patients.
- At 1 year, the composite end-point of death, myocardial infarction (MI) or target vessel revascularisation (TVR) was higher in diabetic patients.
- At 1 year, eptifibatide had a similar effect on these measures in both diabetic and non-diabetic patients.
- The 1-year mortality rate for diabetic patients was higher for those receiving placebo.
- The 1-year mortality rate was similar for diabetic and non-diabetic patients in the eptifibatide group.

Labinaz M, Madan M, O'Shea JC et al (2002) Comparison of one-year outcomes following coronary artery stenting in diabetic versus nondiabetic patients (from the enhanced suppression of the platelet IIb/IIIa receptor with integrilin therapy [ESPRIT] trial). *American Journal of Cardiology* **90**: 585–90

- Rehospitalisation for bleeding events and for either ischaemic or bleeding events was significantly lower in the clopidogrel group.
- The findings demonstrate that there is a greater benefit when using clopidogrel as the primary antiplatelet instead of aspirin.

Bhatt DL, Marso SP, Hirsch AT et al (2002) Amplified benefit to clopidogrel versus aspirin in patients with diabetes mellitus. *American Journal of Cardiology* **90**: 625–8

Clopidogrel is more effective antiplatelet in diabetic patients

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

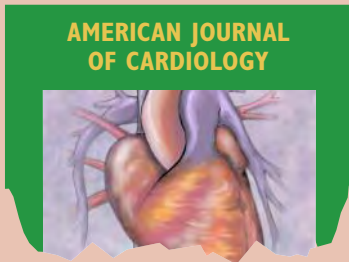
- Patients with diabetes have a higher rate of recurrence of an ischaemic event than do non-diabetic patients.
- Aspirin has a modest benefit over placebo in reducing vascular events in patients with diabetes.
- Clopidogrel has previously been associated with (in the CAPRIE study) a greater relative risk reduction in vascular death, myocardial infarction or ischaemic stroke than aspirin.

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- This study aimed to determine whether clopidogrel had any benefit over aspirin in preventing ischaemic events in patients with diabetes and atherosclerosis.
- The rates of vascular death, myocardial infarction, all-cause stroke, and rehospitalisation for ischaemic events or for bleeding were determined for 3866 patients with diabetes taking either clopidogrel or aspirin in the CAPRIE study.
- The event rate was 15.6% in the clopidogrel group, compared with 17.7% in the aspirin group.

‘QTD might be a useful screening tool for selecting patients with diabetes for further cardiac examinations.’



QT dispersion indicates cardiac abnormalities

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

1 Studies have shown that a prolonged QT dispersion (QTD) is the best predictor of cardiac death in patients with type 2 diabetes.

2 Although the reason for this is unclear, one possibility is that QTD identifies hidden but lethal cardiac abnormalities.

3 This possibility was explored by examining whether any cardiac abnormalities are overrepresented in diabetic patients with a prolonged QTD.

4 Intensive cardiac examinations were carried out on 219 patients with type 2 diabetes.

5 Those with a prolonged QTD had a significantly higher incidence of myocardial ischaemia and left ventricular hypertrophy.

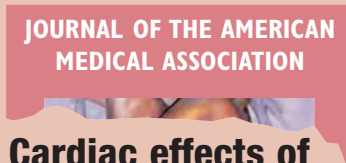
6 The main determinant of a prolonged QTD was found to be ischaemia.

7 QTD increased progressively with the number of different cardiac abnormalities present.

8 This suggests that QTD might be a useful screening tool for selecting patients with diabetes for further cardiac examinations. Such screening could be used to detect a large number of hidden but treatable cardiac abnormalities.

Rana BS, Band MM, Ogston S et al (2002) Relation of QT interval dispersion to the number of different cardiac abnormalities in diabetes mellitus. *American Journal of Cardiology* **90**:483–87

‘Exercise training does more than just improve glycaemic control and reduce blood pressure.’



Cardiac effects of exercise training

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

1 The coexistence of type 2 diabetes and hypertension are bad for cardiovascular health.

2 Most studies of exercise training in people with type 2 diabetes and hypertension focus on glycaemic control and blood pressure reduction.

3 This article reviews the evidence and plausible mechanisms by which exercise training may improve the

cardiovascular health of people with type 2 diabetes and hypertension.

4 Evidence for benefits of exercise training on cardiovascular health is best indicated by improvements in endothelial vasodilator function and left ventricular diastolic function.

5 Exercise training also reduces total and abdominal fat. This leads to improvements in insulin sensitivity and blood pressure and may improve endothelial vasodilator function.

6 The current evidence suggests that exercise training does more than just improve glycaemic control and reduce blood pressure.

Stewart KJ (2002) Exercise training and the cardiovascular consequences of type 2 diabetes and hypertension. Plausible mechanisms for improving cardiovascular health. *Journal of the American Medical Association* **288**: 1622–31



Fluorquinolones reduce CHD risk

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

1 Bacterial infections might be involved in the aetiology of coronary heart disease (CHD). *Chlamydia pneumoniae* is thought to play a role in atherosclerosis.

2 Antibiotics should therefore reduce the risk of CHD developing. An association has previously been found

between fluorquinolones and the risk of myocardial infarction.

3 This study investigated whether antibiotics, particularly fluorquinolones, decreased the risk of CHD in patients with type 2 diabetes.

4 The use of fluorquinolones for >14 days was associated with a lower risk of CHD compared with no use of fluorquinolones.

5 Results suggest that treatment with fluorquinolones reduces the risk of CHD among patients with type 2 diabetes.

Erkens JA, Klungel OH, Herings RMC et al (2002) Use of fluorquinolones is associated with a reduced risk of coronary heart disease in diabetes mellitus type 2 patients. *European Heart Journal* **23**: 1575–9

‘Results suggest that treatment with fluorquinolones reduces the risk of CHD among patients with type 2 diabetes.’

PTCA vs fibrinolysis in diabetic patients

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

1 A retrospective observational study compared early and late outcomes of percutaneous transluminal coronary angioplasty PTCA with fibrinolytic treatment for AMI among patients with diabetes.

2 The sample analysed comprised 202 patients with diabetes and AMI who received reperfusion treatment (99 fibrinolysis and 103 primary PTCA) within 6 hours of symptom onset.



3 Rates for in-hospital recurrent ischaemia and target vessel revascularisation at one year were lower in those treated with PTCA. Death or reinfarction rates were also lower in those treated with PTCA.

4 Among patients with diabetes and AMI, primary PTCA was associated with reduced early and late adverse events compared with fibrinolytic treatment.

Hsu LF, Mak KH, Lau KW et al (2002) Clinical outcomes of patients with diabetes mellitus and acute myocardial infarction treated with primary angioplasty or fibrinolysis. *Heart* **88**: 260–5

HEALTH PSYCHOLOGY



Depression linked to CHD in type 1 diabetes

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

1 Patients with type 1 diabetes are three times more likely to develop depression and 10 times more likely to develop coronary heart disease (CHD) than non-diabetic subjects.

2 It has been suggested that depressive symptomatology may be a risk factor for developing CHD in this population.

3 This study aimed to expand on reports from the Pittsburgh Epidemiology of Diabetes Complications (EDC) Study by examining the association between depression and development of CHD.

4 The EDC study is a natural history study of 658 men and women with childhood-onset type 1 diabetes.

5 Data from the study showed that subjects who reported the fewest depressive symptoms on the Beck Depression Inventory at baseline examination were least likely to develop CHD over 10 years.

6 This relationship might be explained by differences in insulin resistance, autonomic dysregulation, inflammation, smoking and the complications associated with type 1 diabetes.

7 However, it is not known whether depression leads to these disturbances or vice versa. Further research is needed to clarify the pathways between depressive symptomatology, behavioural and physiological processes and CHD.

Kinder LS, Kamarck TW, Baum A, Orchard TJ (2002) Depressive symptomatology and coronary heart disease in type 1 diabetes mellitus: a study of possible mechanisms. *Health Psychology* **21**(6): 542–52

DIABETES RESEARCH AND CLINICAL PRACTICE



C-reactive protein may identify risk of developing CHD

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

1 C-reactive protein (CRP) and interleukin 6 (IL-6) are markers of systemic inflammation. It is thought that they could be used to identify people at risk of coronary heart disease (CHD).

2 This study examined the relationship of CRP and IL-6 with CHD risk factors in 55 patients with type 2 diabetes with CHD and 51 age- and sex-matched type 2 diabetic patients without CHD (controls).

3 Participants were assayed for CRP, IL-6, total plasma homocysteine (tHcy), lipoprotein (a) [Lp(a)] and sialic acid (SA).

4 Multivariate and logistic regression analyses were used to relate these markers with CHD risk factors.

5 CRP ($P=0.02$) and tHcy ($P=0.03$) were significantly higher in patients with CHD than in controls, even after correction for age and sex.

6 There was no significant difference between the two groups for IL-6, Lp(a), SA or lipid parameters.

7 Partial correlation analyses of CRP and IL-6 with other variables showed significant correlation of CRP with tHcy and SA only in the subjects with CHD.

8 These results support the inclusion of CRP (high-sensitivity assay) in the risk assessment of patients with type 2 diabetes.

Mojiminiyi OA, Abdella N, Moussa MA et al (2002) Association of C-reactive protein with coronary heart disease risk factors in patients with type 2 diabetes mellitus. *Diabetes Research and Clinical Practice* **58**: 37–44

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY



Atherosclerosis more prevalent in diabetic patients

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

1 People with diabetes but without clinical coronary artery disease (CAD) have a similar cardiovascular mortality to non-diabetic people with clinical CAD, but the reason for the excess mortality is not clear.

2 This study examined the link between diabetes and coronary atherosclerosis among a defined autopsied population in the US.

3 The prevalence of atherosclerosis in the population was analysed using a global coronary score and prevalence of high-grade stenoses.

4 Almost 75% of those with diabetes but without clinical CAD had high-grade coronary atherosclerosis, and more than 50% had multivessel disease.

5 Among those without diabetes, women had less atherosclerosis than men, whereas among those with diabetes the incidence of atherosclerosis was the same.

6 Subjects with diabetes but without clinical CAD and non-diabetic subjects with clinical CAD had a similar global coronary disease burden and prevalence of high-grade atherosclerosis.

7 These findings show that people with diabetes are at increased risk of clinical CAD, highlighting the need for aggressive prevention of atherosclerosis in all people with diabetes.

Goraya TY, Leibson CL, Palumbo PJ et al (2002) Coronary atherosclerosis in diabetes mellitus: a population-based autopsy study. *Journal of the American College of Cardiology* **40** (5): 946–53

‘Subjects who reported the fewest depressive symptoms on the Beck Depression Inventory at baseline examination were least likely to develop CHD over 10 years.’

‘C-reactive protein ($P=0.02$) and total plasma homocysteine ($P=0.03$) were significantly higher in patients with CHD than in controls...’

‘Findings... highlight the need for aggressive prevention of atherosclerosis in all people with diabetes.’