

Cardiovascular journals

EUROPEAN HEART JOURNAL



ACE inhibitors reduce risk of CV events in people with vascular disease

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

1 Several studies have shown the benefits of angiotensin-converting enzyme (ACE) inhibitor therapy in differing groups of people, including those with diabetes.

2 The authors of this study analysed data from three large studies investigating the treatment effects of perindopril-based therapy on people with, or at high-risk of, vascular disease (ADVANCE, EUROPA and PROGRESS).

3 The study cohort comprised 29 463 individuals who were randomly assigned to either placebo or perindopril-based treatment. All-cause mortality and major cardiovascular (CV) outcomes were recorded during approximately 4 years follow-up.

4 ACE inhibitor therapy was associated with a significant reduction in all-cause mortality ($P=0.006$), CV mortality ($P=0.004$), non-fatal myocardial infarction ($P<0.001$), stroke ($P=0.002$), and heart failure ($P=0.015$).

5 These results were consistent across the groups involved in the studies: people with diabetes, people with coronary artery disease, and people with stroke or transient ischaemic attack.

6 The authors recommended that ACE inhibitor therapy be used for CV protection in those at risk of developing, or suffering from, vascular disease.

Brugts JJ, Ninomiya T, Boersma E et al (2009) The consistency of the treatment effect of an ACE-inhibitor based treatment regimen in patients with vascular disease or high risk of vascular disease: a combined analysis of individual data of ADVANCE, EUROPA, and PROGRESS trials. *Eur Heart J* **30**: 1385–94

Judicious use of ACE inhibitors: No time to waste?



Vinod Patel, Consultant Physician at the George Eliot Hospital, Nuneaton, and Associate Professor at the University of Warwick

Brugts and colleagues (summarised alongside) have produced a valuable meta-analysis of the effects of perindopril-based treatments in people at high risk of CVD. This is a valuable addition to the meta-analysis published by Dagenais et al in 2006, which

studied three trials using perindopril (EUROPA; Fox et al, 2003), ramipril (HOPE; Heart Outcomes Prevention Evaluation Study Investigators, 2000) andtrandolapril (PEACE; Braunwald et al, 2004).

Results from all these trials are entirely consistent. There is a significant reduction in myocardial infarction, stroke, cardiovascular death, and all-cause mortality. HOPE, in its diabetes sub-group – the MICRO-HOPE study – specifically shows a reduction in heart failure and overt nephropathy with a trend towards a reduction in laser photocoagulation treatment for sight-threatening diabetic retinopathy.

I think that time should not be wasted pontificating whether the treatment benefits of an ACE-inhibitor are due to a small reduction in blood pressure (HOPE 3/2 mmHg, EUROPA 4.5/3 mmHg) or a “magical”

specific effect inherent to the class of angiotensin-converting enzyme (ACE) inhibitors. It is clear that the majority of people with type 1 and type 2 diabetes will benefit from ACE-inhibitors. The specific cohorts that were included in these trials differed from trial to trial. ACE inhibitors, and indeed angiotensin-receptor antagonists and statins, should never be used in women in reproductive potential because of the 15% risk of serious fetal malformation.

However, it is reasonable to conclude that most people with diabetes, over the age of 50, should be considered for ACE-inhibitor therapy, particularly as the cost of these agents is so low and benefits so well substantiated.

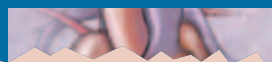
Braunwald E, Domanski MJ, Fowler SE et al (2004) Angiotensin-converting-enzyme inhibition in stable coronary artery disease. *N Engl J Med* **351**: 2058–68

Dagenais GR, Pogue J, Fox K et al (2006) Angiotensin-converting-enzyme inhibitors in stable vascular disease without left ventricular systolic dysfunction or heart failure: a combined analysis of three trials. *Lancet* **368**: 581–8

Fox KM, EUROpean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease Investigators (2003) Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study). *Lancet* **362**: 782–8

Heart Outcomes Prevention Evaluation Study Investigators (2000) Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. *Lancet* **355**: 253–9

CIRCULATION



CV risk factors in people with diabetes versus those without

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

1 Trends in BMI, blood pressure, smoking and cholesterol among people with and without type 2 diabetes were examined by the authors using data from the Framingham Heart Study between 1970 and 2005.

2 At the study start, 4195 participants (3990 without diabetes and 205 with diabetes) were aged 50, and 3495 (3178 without diabetes and 317 with diabetes) were aged 60.

3 Among 50-year-old people without diabetes, there was an increase in BMI of 0.39 kg/m² per 10 years, whereas for those with the condition, there was an increase of 2.52 kg/m² ($P<0.001$).

4 The mean decrease in LDL-cholesterol for people without diabetes was 7.43 mg/dL over 10 years, and 15.5 mg/dL for those with the condition ($P=0.002$).

5 For systolic blood pressure, the mean decrease in those without diabetes was 3.35 mmHg per decade and 3.50 mmHg for people with diabetes ($P=$ non-significant).

6 Risk factors for major CV disease events have improved in people with diabetes, but the burden is still greater than those without the condition.

Preis SR, Pencina MJ, Hwang SJ et al (2009) Trends in cardiovascular disease risk factors in individuals with and without diabetes mellitus in the Framingham Heart Study. *Circulation* **120**: 212–20

“HbA_{1c} level is not associated with cardiac outcomes in people with advanced coronary artery disease and diabetes.”

AMERICAN JOURNAL OF CARDIOLOGY



Pioglitazone therapy improves HDL-cholesterol and triglyceride levels

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

1 The Prospective Pioglitazone Clinical Trial in Macrovascular Events (PROactive) trial was a long-term, randomised, double-blind, cardiovascular outcomes study in people with type 2 diabetes at high cardiovascular risk who had pioglitazone or placebo added to existing treatment.

2 The authors of this study examined the effect of pioglitazone on triglycerides, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol levels to determine whether pioglitazone-induced lipid effects were altered by antidiabetes medication or statin therapy in the PROactive cohort.

3 This post-hoc analysis found that triglyceride levels decreased in all subgroups treated with pioglitazone (−9.9% to −12.3%), independently of antidiabetes drugs or statin therapy. No significant change was observed in the placebo group.

4 HDL-cholesterol levels were almost doubled in people taking antidiabetes or statin therapy compared with placebo, although LDL-cholesterol levels did increase slightly more in than in the placebo group.

5 The authors concluded that long-term pioglitazone therapy may improve lipid parameters, regardless of baseline antidiabetes therapy or statin use.

Spanheimer R, Betteridge DJ, Tan MH et al (2009) Long-term lipid effects of pioglitazone by baseline anti-hyperglycemia medication therapy and statin use from the PROactive experience (PROactive 14). *Am J Cardiol* **104**: 234–9

AMERICAN JOURNAL OF CARDIOLOGY



HbA_{1c} is not a predictor of MACE

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

1 In this study, the authors sought to determine the efficacy of HbA_{1c} as a prognostic tool for predicting major adverse cardiovascular events (MACEs) in people with diabetes.

2 Between 2002 and 2007, 352 people with diabetes consecutively

underwent percutaneous coronary intervention. Of these, 429 had an HbA_{1c} level <7% (<53 mmol/mol; Group A), and 523 had an HbA_{1c} level >7% (>53 mmol/mol; Group B).

3 BMI was higher in Group B ($P=0.03$), and individuals in this group were also more likely to be receiving insulin therapy ($P<0.001$). Occurrence of MACEs was similar in the two groups (23.7% vs. 20.8%).

4 The authors concluded that HbA_{1c} level is not associated with cardiac outcomes in people with advanced coronary artery disease and diabetes.

Lemesle G et al (2009) Prognostic value of hemoglobin A1C levels in patients with diabetes mellitus undergoing percutaneous coronary intervention with stent implantation. *Am J Cardiol* **104**: 41–5

AMERICAN JOURNAL OF CARDIOLOGY



Diabetes linked to higher risk of poor outcomes and death

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

1 The authors of this article aimed to ascertain the long- and short-term cardiovascular outcomes in people with diabetes experiencing acute ischaemic chest pain.

2 Between 1 January 1985 and 31 December 1992, 2271 people were followed-up for a median of 16.6 years. Of these, 336 had diabetes.

3 The primary outcome for the study was long-term all-cause mortality; secondary outcomes were major adverse cardiovascular and cerebrovascular events (MACCEs) and heart failure at 30 days and at a median of 7.3 years.

4 The 30-day rate of MACCEs was 10.1% in people with diabetes and 6.1% in those without ($P=0.007$). Heart failure was more common in people with diabetes at 30 days (9.8% vs 3.1%; $P<0.001$). Over 7.3 years, 272 people with diabetes (81.9%) died vs. 936 (49.2%) without diabetes ($P<0.001$)

5 People with diabetes have a higher short-term risk of MACCEs and poorer long-term survival than people without diabetes.

Farkouh ME et al (2009) Usefulness of diabetes mellitus to predict long-term outcomes in patients with unstable angina pectoris. *Am J Cardiol* **104**: 492–7

HEART



Elevated HbA_{1c} level predicts mortality

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

1 This study was undertaken to determine the prognostic value of HbA_{1c} testing in people with suspected heart failure who do not have diabetes.

2 Of 970 people without diabetes referred to a heart failure clinic between 2001 and 2004, 45% had

left ventricular ejection fraction (LVEF) ≤45%, and 50% had an HbA_{1c} level >6% (>42 mmol/mol).

3 An increase in mortality was seen in people with LVEF ≤45% with an HbA_{1c} level >6.7% (50 mmol/mol; $P<0.001$) compared with people with lower levels.

4 One-year mortality was 26.5% in those with an elevated HbA_{1c} level versus 9.4% in those with lower levels. HbA_{1c} could be a useful risk stratification tool in people with LVEF ≤45%.

Goode KM et al (2009) Elevated glycated haemoglobin is a strong predictor of mortality in patients with left ventricular systolic dysfunction who are not receiving treatment for diabetes mellitus. *Heart* **95**: 917–23