

## Cardiovascular journals

### A role for retinopathy in predicting cardiovascular disease



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There continues to be interest in the link between diabetic retinopathy and cardiovascular (CV) disease. A number of studies, mainly cross-sectional, have suggested that the severity of retinopathy indicates the severity of

CV disease. However, the association has often been rendered insignificant following adjustment for other CV risk factors.

Recently, Gimeno-Orna et al (2009; summarised alongside) published a study that assessed the association between retinopathy and incident CV events in people with type 2 diabetes. Participants underwent measurement of clinical and biochemical variables and were followed-up for a mean of 6.7±2.6 years. Two clinical endpoints were assessed: fatal and non-fatal

CV events, consisting of unstable angina, including revascularisation, non-fatal or fatal myocardial infarction, transient ischaemic attack, non-fatal or fatal stroke, lower-leg amputation, terminal chronic heart failure and sudden death.

The results suggest a significant relationship. Incident CV event rates were 30.7 per 1000 patient years for those with a normal fundus, 56.7 for those with non-proliferative retinopathy, and 90.7 in those with proliferative retinopathy ( $P<0.0001$ ). Further, both non-proliferative and proliferative retinopathy were significantly associated with incident CV disease ( $P=0.028$  and  $P=0.05$ , respectively).

Gimeno-Orna's et al (2009) findings further support the notion of an independent link between retinopathy and incident CV disease. Consequently, retinopathy may need to be incorporated into CV risk factor assessment for type 2 diabetes.

**“Retinopathy may need to be incorporated into cardiovascular risk factor assessment for type 2 diabetes.”**

### AMERICAN JOURNAL OF CARDIOLOGY

#### Retinopathy is an independent predictor of CV events

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- In this study, the authors assessed the independent contribution made by retinopathy to cardiovascular (CV) events in people with type 2 diabetes.
- Participants ( $n=458$ ) were consecutively recruited between 1994 and 1998 from a Spanish hospital, had both type 2 diabetes and a visible fundus at baseline.
- Clinical and biochemical variables, including urinary albumin excretion rate, were measured. Participants were followed-up for a mean of 6.7±2.6 years.
- Both fatal and non-fatal CV events were taken as clinical endpoints. Hazard ratios (HR) and relative risk were used to evaluate each variable.

- Participants with a normal fundus experienced a CV event rate of 30.7 per 1000 patient years, compared with 90.7 in those with proliferative retinopathy ( $P<0.0001$ ).
- Following multivariate analysis, both non-proliferative (HR 1.6, 95% confidence interval [CI] 1.1–2.5;  $P=0.028$ ) and proliferative (HR 2, 95% CI 1.1–3.1;  $P=0.05$ ) retinopathy were found to be significantly and independently associated with CV events.
- This study showed an independent association between baseline retinopathy and CV events, irrespective of other established CV risk factors, remaining significant after adjustment for microvascular and macrovascular complications.

Gimeno-Orna JA, Faure-Nogueras E, Castro-Alonso FJ, Boned-Juliani B (2009) Ability of retinopathy to predict cardiovascular disease in patients with type 2 diabetes mellitus. *Am J Cardiol* **103**: 1364–7

### EUROPEAN HEART JOURNAL

#### Life-expectancy tables highlight modifiable risk

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

- In an effort to provide a prognostic indicator tool for clinicians and people with diabetes, the authors developed life-expectancy tables that illustrated the association between life-expectancy and the major modifiable risk factors of type 2 diabetes.

- Based on parametric proportional hazards risk equations that estimate

the mortality and vascular complications of diabetes, life-expectancy tables were stratified by age–sex groups and developed for combinations of modifiable risk factors.

- Positive modification of major risk factors (for example, smoking, blood pressure, cholesterol, HbA<sub>1c</sub>) was found to increase the life-expectancy of a 55-year-old man with diabetes from 13.2 years to 21.1 years.

- The authors suggest that life-expectancy tables are a useful tool for conveying prognostic information about the longevity associated with improving modifiable risk factors to people with type 2 diabetes.

Leal J, Gray AM, Clarke PM (2009) Development of life-expectancy tables for people with type 2 diabetes. *Eur Heart J* **30**: 834–9

CIRCULATION

**Role for HDL-raising therapies in improving glycaemia**

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

**1** HDL is associated with protection from adverse cardiovascular outcomes in large trials. Type 2 diabetes, as well as the associated pathologies of obesity, insulin intolerance and high plasma triglycerides, is associated with low and dysfunctional HDL.

**2** The authors investigated the role of HDL on glucose metabolism, hypothesising that HDL modulates plasma insulin and activates skeletal muscle adenosine monophosphate-activated protein kinase, a key metabolic regulatory enzyme.

**3** In this double-blind, controlled, crossover study, participants ( $n=13$ ) with type 2 diabetes received intravenous reconstituted HDL (rHDL; 80 mg/kg over 4 hours) and placebo, on separate days,  $\geq 4$  weeks apart. Participants were withdrawn from any medications that could have affected the outcomes measured.

**4** Treatment with rHDL saw a fall from baseline in plasma glucose greater than that of placebo (at 4 hours: rHDL  $-2.6 \pm 0.4$  mmol/L; placebo  $-2.1 \pm 0.3$  mmol/L;  $P=0.018$ ), and an increase in plasma insulin (at 4 hours: rHDL  $3.4 \pm 10.0$  pmol/L; placebo  $-19.2 \pm 7.4$  pmol/L;  $P=0.034$ ).

**5** The authors concluded that the reduction in plasma glucose, and increase in insulin achieved, suggest a role for HDL-raising therapies, beyond atherosclerosis, for the treatment of hyperglycaemia in type 2 diabetes.

Drew BG, Duffy SJ, Formosa MF et al (2009) High-density lipoprotein modulates glucose metabolism in patients with type II diabetes mellitus. *Circulation* **119**: 2103–11

AMERICAN JOURNAL OF CARDIOLOGY

**Higher mortality for people with diabetes 1-year after ACS**

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

**1** Management and outcomes in people with and without diabetes, and acute coronary syndrome (ACS), were evaluated using a multinational survey of 6385 participants (1587 with diabetes) with ACS.

**2** People with diabetes were found to have received more treatment for acute symptoms, but fewer treatments that have proven impact on outcome; there was a non-significant association between diabetes and in-hospital mortality (odds ratio [OR] 1.05, 95% confidence interval [CI] 0.78–1.42), but a significant association with mortality at 1 year (OR 1.37, 95% CI 1.09–1.71).

**3** The authors concluded that diabetes coupled with ACS has deleterious long-term implications and risk-modifying treatments should be considered.

Hasin T, Hochadel M, Gitt AK et al (2009) Comparison of treatment and outcome of acute coronary syndrome in patients with versus patients without diabetes mellitus. *Am J Cardiol* **103**: 772–8

AMERICAN HEART JOURNAL

**Glycaemia a stronger predictor of death than history of diabetes following MI**

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

**1** The authors retrospectively compared the prognostic value of in-hospital blood glucose levels with that of diabetes history in 30 536 participants following an acute myocardial infarction (AMI).

**2** The average in-hospital blood glucose (mean from admission, 6 and 24 hours), diabetes history, and death at 30 days were documented.

**3** Following adjustment for a history of diabetes, average blood glucose predicted 30-day death ( $P<0.0001$ ); diabetes history alone predicted 30-day death ( $P<0.0001$ ), but lost significance following adjustment for average glucose ( $P=0.72$ ).

**4** In-hospital blood glucose levels are a stronger predictor of death following AMI than diabetes history.

Goyal A, Mehta SR, Gerstein HC et al (2009) Glucose levels compared with diabetes history in the risk assessment of patients with acute myocardial infarction. *Am Heart J* **157**: 763–70

AMERICAN HEART JOURNAL

**Preoperative OGTT predicts long-term outcomes following vascular surgery**

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

**1** The role of preoperative oral glucose tolerance testing (OGTT) in addition to fasting glucose levels in people undergoing vascular surgery was assessed to predict long-term cardiovascular (CV) outcomes.

**2** Participants ( $n=404$ ) without a history of impaired glucose tolerance (IGT) or diabetes were tested, and 104 and 43, respectively, were diagnosed preoperatively and followed-up for a median of 3 years.

**3** Multivariate analysis showed that those with IGT had an increased risk of CV events (hazard ratio [HR] 2.77, 95% confidence interval [CI] 1.83–4.20) and mortality (HR 2.06, 95% CI 1.03–4.12).

**4** The authors suggested that all vascular surgery patients should be tested for glucose regulation disorders before surgery.

van Kuijk JP, Dunkelgrun M, Schreiner F et al (2009) Preoperative oral glucose tolerance testing in vascular surgery patients: long-term cardiovascular outcome. *Am Heart J* **157**: 919–25

**“In-hospital blood glucose levels are a stronger predictor of death following acute myocardial infarction than diabetes history.”**

“People with diabetic nephropathy who received clopidogrel experienced significantly increased all-cause and cardiovascular mortality compared with those who received placebo.”

## AMERICAN JOURNAL OF CARDIOLOGY

### Diabetes duration linked to left ventricular diastolic dysfunction

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

**1** Preclinical left ventricular (LV) diastolic dysfunction, independent of coronary disease or hypertension, has been linked to diabetes by several studies. Here, the authors sought to determine the nature of the relationship between LV diastolic dysfunction and duration of diabetes.

**2** A group of 486 participants with diabetes from the US, who were free of heart failure, and a subsequent tissue Doppler echocardiographic assessment of diastolic function, were the study population.

**3** Time from diabetes diagnosis to echocardiogram, using simple linear regression and following adjustment (age, gender, BMI, previous coronary disease, previous hypertension, and ejection fraction) showed that the ratio of early mitral velocity to medial mitral annulus velocity, for every 1 year after the onset of diabetes, increased by 0.23 (95% confidence interval [CI] 0.16–0.30;  $P=0.007$ ).

**4** A duration of diabetes  $\geq 4$  years was independently associated with LV diastolic dysfunction after adjustment for age, gender, BMI, previous coronary disease, previous hypertension, and ejection fraction (odds ratio 1.91, 95% CI 1.19–3.07;  $P=0.007$ ).

**5** Duration of diabetes was shown to correlate with significant LV diastolic dysfunction, which is predictive of all-cause mortality and is independent of coronary disease and hypertension.

From AM, Scott CG, Chen HH (2009) Changes in diastolic dysfunction in diabetes mellitus over time. *Am J Cardiol* **103**: 1463–6

## EUROPEAN HEART JOURNAL

### Atrial fibrillation needs aggressive risk management in diabetes

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

**1** Atrial fibrillation (AF) is common in people with diabetes. In this study the authors investigated the clinical outcomes associated with, and the impact of routine blood pressure lowering on, AF in people with type 2 diabetes.

**2** As part of the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicon-MR Controlled Evaluation) study, participants ( $n=11\ 140$ ) were randomised to receive placebo or a fixed combination of perindopril and indapamide and followed-up for 4.3 years.

**3** Differences between mortality and cardiovascular (CV) disease outcomes between those with and without AF (7.6% of participants had AF at baseline) were assessed.

**4** AF was associated with a 61% higher risk of all-cause mortality ( $P<0.0001$ ), and was a comparable higher risk of CV death, stroke, and heart failure (all  $P<0.001$ ).

**5** Those with AF randomised to receive perindopril and indapamide experienced a greater absolute risk reduction for all-cause and CV death, compared with those without AF (one death/ per 39 people with AF prevented with 5 years of active therapy, compared to 1 death per 84 in those without AF).

**6** The authors concluded that those with diabetes and AF are at greater risk of death and CV event, and greater absolute benefits from blood pressure-lowering treatment can be achieved in this group.

Du X, Ninomiya T, de Galan B et al (2009) Risks of cardiovascular events and effects of routine blood pressure lowering among patients with type 2 diabetes and atrial fibrillation: results of the ADVANCE study. *Eur Heart J* **30**: 1128–35

## AMERICAN JOURNAL OF CARDIOLOGY

### Clopidogrel harmful in people with diabetic nephropathy

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

**1** Identifying a gap in the literature, the authors of this prospective randomised study aimed to assess the risks and benefits of long-term clopidogrel therapy in people with diabetic nephropathy.

**2** The authors performed a post-hoc analysis of data obtained in the CHARISMA (Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance) randomised controlled trial.

**3** Participants without active acute coronary syndrome but with established atherosclerotic disease (symptomatic) or multiple risk factors for atherosclerotic disease (asymptomatic) were randomised to receive either clopidogrel plus aspirin ( $n=1006$ ) or placebo plus aspirin ( $n=1003$ ).

**4** Those with diabetic nephropathy who received clopidogrel experienced significantly increased all-cause and cardiovascular mortality (hazard ratio [HR] 1.8, 95% confidence interval [CI] 1.2–2.7;  $P=0.006$ ) compared with those who received placebo (HR 1.7, 95% CI 1.0–2.9;  $P=0.028$ ).

**5** This analysis suggests that treatment with clopidogrel may be harmful in people with diabetic nephropathy, and the authors call for additional studies to further investigate this possible interaction.

Dasgupta A, Steinhubl SR, Bhatt DL et al (2009) Clinical outcomes of patients with diabetic nephropathy randomized to clopidogrel plus aspirin versus aspirin alone (a post hoc analysis of the clopidogrel for high atherothrombotic risk and ischemic stabilization, management, and avoidance [CHARISMA] trial). *Am J Cardiol* **103**: 1359–63