

## Diabetes journals

### Is the severity and progression of diabetic retinopathy linked to incident cardiovascular disease?



Jiten Vora, Professor of Diabetes, Royal Liverpool University Hospital, Liverpool

There is considerable data demonstrating the association of

retinopathy, and its severity, to vascular disease.

This is a further study

that evaluates the presence of diabetic retinopathy and its severity to incident cardiovascular disease. The

study by Gerstein et al (summarised alongside) demonstrates that both the severity of retinopathy and its progression are determinants

of incident cardiovascular outcomes. Adjusted hazard ratios (HRs) for cardiovascular disease were, in fact, lower in people who had mild

retinopathy (hazard ratio [HR] 1.4; 95% CI, 1.12–1.97) and higher in people with severe retinopathy (HR 2.35; 95% CI, 1.47–3.76).

Therefore, this study provides the practising clinician with further evidence that retinopathy, both its presence and progression, could well be

used as a risk factor in determining medication for cardiovascular risk factor reduction in people with T2D.

**“The study demonstrates that both the severity of retinopathy and its progression are determinants of incident cardiovascular outcomes.”**

### DIABETES CARE

### Is DR progression predictive of CV events?

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

1 Although it has already been established that the severity of diabetic retinopathy (DR) correlates with the development of cardiovascular (CV) events, little is known about whether the progression of DR is associated with the onset of adverse CV outcomes.

2 CV outcomes (CV death, stroke and non-fatal myocardial infarction) were prospectively analysed in conjunction with DR progression in 3433 participants over a period of 4 years. Participants were enrolled as a part of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial.

3 Within the cohort, the authors classified retinopathy as absent, mild, moderate or severe and progression was defined as a <2-step, 2–3-step or >3-step change from baseline retinopathy.

4 The authors found that the adjusted hazard ratios (HRs) for CV outcome were lower in those who had mild retinopathy (HR 1.49; 95% CI, 1.12–1.97) and higher in those with severe retinopathy (HR 2.35; 95% CI, 1.47–3.76).

5 As retinopathy became more severe, each category of change was associated with a 38% increase in the hazard of CV outcomes (HR 1.38; 95% CI, 1.10–1.74). The relationship between DR progression and CV outcomes was non-significant after adjusting for baseline and follow-up HbA<sub>1c</sub>, systolic blood pressure, and lipid levels.

6 The authors concluded that severity and progression of retinopathy may be predictive of adverse CV outcomes.

Gerstein HC, Ambrosius WT, Danis R et al (2013) Diabetic retinopathy, its progression, and incident cardiovascular events in the ACCORD trial. *Diabetes Care* **36**: 1266–71

### DIABETES CARE

### Aggressive blood pressure control may increase the risk of CHD

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

1 People with diabetes have an increased risk of coronary heart disease (CHD). Although it is known that reduced blood pressure can lower the risk of CHD in these individuals, few studies have investigated whether the smallest risk of CHD is found in those with the lowest blood pressure.

2 The authors conducted a prospective cohort analysis on 17 536 African American and 12 618 white people with diabetes. A Cox proportional hazards regression model was applied to evaluate the relationship between blood pressure and CHD risk.

3 In total, 7260 incidents of CHD were identified over the 6-year follow-up. In both African American and white people, an age-dependant

U-shaped association was observed between systolic and diastolic blood pressure with CHD risk at baseline and follow-up ( $P < 0.001$ ).

4 The U-shaped association was observed in those aged 30–39 years and 50–59 years, but those  $\geq 60$  years displayed an inverse association.

5 For African Americans with diabetes, hazard ratios for CHD and baseline blood pressure (>110/65 mmHg, 110–119/65–69, 120–129/70–80, and 130–139/80–90 mmHg [reference group] 140–159/90–100 and  $\geq 160/100$  mmHg) were 1.73, 1.16, 1.04, 1.00, 1.06 and 1.11 and 1.60, 1.27, 1.08, 1.00, 0.95, and 0.99 for white people with diabetes ( $P < 0.001$  for all).

6 The authors concluded that an age dependant U-shaped and inverse relationship exists between blood pressure and CHD risk, whereby tight blood pressure control (blood pressure equal to 120/70 mmHg) is significantly correlated with an elevated risk of CHD.

Zhao W, Katzmarzyk PT, Horswell R et al (2013) Aggressive blood pressure control increases coronary heart disease risk among diabetic patients. *Diabetes Care* 11 Jun [Epub ahead of print]

## DIABETES

### Previous HbA<sub>1c</sub> exposure influences cardiac structure and function

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

1 Results from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study suggest that intensive glycaemic treatments are associated with a reduced incidence of cardiovascular disease in people with diabetes.

2 The authors sought to determine if cardiac function and structure, as measured in the EDIC study, were altered as a result of intensive therapy received by participants in the DCCT study.

3 Participants with T1D were followed-up for 15 years following an initial 6.5 years of intensive or conventional therapy. Of the 1371 people enrolled in the DCCT study, cardiac magnetic resonance (CMR) was carried out on 1017 participants.

4 No significant differences were detected in the aortic distensibility (AD), end diastolic volume (EDV), end systolic volume (SDV), stroke volume (SV), left ventricular (LV) mass, ejection fraction, LV mass/EDV or cardiac output (CO) between DCCT participants receiving conventional and intensive treatment.

5 A significant correlation between mean HbA<sub>1c</sub>, AD, LV mass, EDV, SV, CO and LV mass/EDV was reported, even after cardiovascular disease factors were accounted for.

6 The authors concluded that cardiac function and remodelling in the EDIC cohort was associated with previous exposure to HbA<sub>1c</sub> and not treatment regimen during the DCCT study.

Genuth S, Backlund JY, Bayless M et al (2013) Effects of prior intensive versus conventional therapy and history of glycemia on cardiac function in type 1 diabetes in the DCCT/EDIC. *Diabetes* 21 Mar [Epub ahead of print]

## DIABETES CARE

### Increased IMT in youth with T1D

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

1 Previous research has shown that adults with T1D have increased carotid intima-media thickness (IMT), although this association is yet to be explored in young people with T1D.

2 With the use of ultrasound, IMT was measured in young people aged 18.9 ± 3.3 years with (n=402) and without (n=206) diabetes, who were matched by age, sex and ethnicity.

3 Greater bulb IMT was observed in young people with T1D, even after adjusting for variables such as demographics and cardiovascular risk factors (P=0.01).

4 Other determining factors of IMT included age, gender, systolic blood pressure and adiposity. Case-control differences in IMT disappeared after adjusting for HbA<sub>1c</sub>, indicating that hyperglycaemia may be the cause of elevated IMT values in participants.

5 The authors concluded that within the study cohort, youth with T1D had a greater IMT compared to those without diabetes.

Urbina EM, Dabelea D, D'Agostino RB Jr et al (2013) Effect of type 1 diabetes mellitus on carotid structure and function in adolescents and young adults. *Diabetes Care* 5 Apr [Epub ahead of print]

## DIABETOLOGIA

### Accurate predictions: UKPDS

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

1 The authors aimed to assess the efficacy of the UK Prospective Diabetes Study (UKPDS) Outcomes Model by comparing the rates of observed mortality compared to that predicted by the model.

2 The incidence of T2D-associated mortality and complications were analysed over a 17-year period using data

from Italian participants enrolled in the Casale Monferrato Survey.

3 Predicted and observed risks of all-cause mortality were identical at years 5 (23%) and 6 (47%), but was overestimated at 15 years (an estimate of 67% versus 64% observed, 95% CI, 61–66%). Myocardial infarction and congestive heart failure were accurately predicted. The model was most effective in people with a shorter diabetes duration.

4 The authors concluded that the UKPDS model is effective in predicting mortality in people with T2D, although external validation is required.

Pagano E, Gray A, Rosato R et al (2013) Prediction of mortality and macrovascular complications in type 2 diabetes. *Diabetologia* 17 May [Epub ahead of print]

## DIABETES CARE

### T2D and arterial stiffening

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

1 The authors investigated the haemodynamic factors associated with central pulse pressure (PP) in people with T2D, and if abnormalities in central PP are also observed in people with impaired fasting glucose (IFG).

2 An increased mean arterial pressure (MAP) was found to be associated

with IFG but not with aortic stiffening or abnormal aortic pulsatile indices.

3 T2D was significantly correlated with elevated aortic root characteristic impedance, aortic root elastance-thickness product, aortic root pulse wave velocity, carotid-femoral pulse wave velocity, as well as a reduced total arterial compliance and wave reflection.

4 The authors concluded that increased arterial stiffness, but not aortic root diameter or carotid stiffness, was associated with T2D and not IFG.

Chirinos JA, Segers P, Gillebert TC et al (2013) Central pulse pressure and its hemodynamic determinants in middle-aged adults with impaired fasting glucose and diabetes. *Diabetes Care* Apr 22 [Epub ahead of print]

**“Greater bulb intima-media thickness (IMT) was observed in young people with T1D, even after adjusting for variables such as demographics and cardiovascular risk factors (P=0.01).”**