### Clinical DIGEST 3

#### **Cardiovascular journals**

#### AMERICAN JOURNAL OF CARDIOLOGY

### Diabetes not a CHD risk equivalent

- Previous studies have shown that people with T2D without a history of coronary heart disease (CHD) have the same risk of CV events as those without diabetes who have a history of CHD.
- This study aimed to determine CV event rates in people with and without diabetes from the REACH (Reduction of Atherothrombosis for Continued Health) registry an international, contemporaneous cohort of 68 236 outpatients (44% of whom had T2D) with risk factors of, or established, coronary artery disease, cerebrovascular disease, peripheral vascular disease or multiple risk factors for vascular disease (major adverse CV events [MACEs]).
- The MACE rate at 1 year was positively associated with the number of atherothrombotic sites in people with and without diabetes, with a higher rate in individuals with diabetes than those without (3.8% vs 3.0%; *P*<0.001).
- People with diabetes with risk factors only had a lower MACE rate than individuals without diabetes or those with diabetes who had established atherothrombotic disease (2.2% vs 4.0% vs 6.0%, respectively; *P*<0.001).
- Individuals with diabetes in the REACH Registry have a substantially greater risk of CV events than those without diabetes in relation to the number of atherothrombotic sites.
- The authors concluded that, although increasing risk, T2D may not be truly equivalent to previous atherothrombotic events in predicting new CV event rates.

Krempf M, Parhofer KG, Steg G et al (2010) Cardiovascular event rates in diabetic and nondiabetic individuals with and without established atherothrombosis (from the Reduction of Atherothrombosis for Continued Health [REACH] Registry). *Am J Cardiol* **105**: 667–71

#### Diabetes – a coronary heart disease risk equivalent?



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t is widely recognised that people with T2D are at high risk of cardiovascular (CV) disease (CVD), with T2D considered to be a risk-factor equivalent to coronary heart disease (CHD) by many (National Cholesterol Education

Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults [Adult Treatment Panel III], 2002). However, there remains considerable debate as to whether T2D confers the same CV risk as established CV disease.

The objective of the study summarised alongside (Krempf et al, 2010) was to determine CV event rates in people with and without diabetes from the REACH (Reduction of Atherothrombosis for Continued Health) Registry with established coronary heart, cerebrovascular or peripheral vascular disease, or multiple CV risk-factors.

The REACH Registry is a large, robust, international and contemporary sample of outpatients with either risk factors for CVD or established CVD, and thus provides a unique

opportunity to gain an understanding of the epidemiology of atherosclerotic vascular disease in people with and without diabetes.

After 1 year of follow-up, the overall event rate was higher in those with (3.8%), than in those without (3%), diabetes (P<0.001). Individuals with diabetes and CV risk factors had a lower CV event rate than individuals, with or without diabetes, who had established CVD (2.2% vs 6.0% vs 4.0%, respectively).

These observations illustrate that people with diabetes and established CVD are at the highest risk of further CV events, while diabetes *per se* cannot be considered a CHD risk equivalent. However, within the group as a whole, people with diabetes experienced a higher CV event rate. It is also noteworthy that event rates, even in the highest risk group, were relatively low, illustrating the utility of multiple risk-factor management.

The key conclusion from this study, however, is that prevention is better than cure when it comes to atherothrombotic vascular disease in people with T2D.

National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (2002) Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 106: 3143–421

#### JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

# Increased insulin resistance following atorvastatin therapy

This randomised, placebocontrolled study was designed to determine whether atorvastatin decreased insulin sensitivity, and increase ambient glycaemia, in people with hypercholesterolaemia.

Participants received placebo or atorvastatin daily in 10, 20, 40 and 80 mg doses, respectively, during a 2-month treatment period.

- Atorvastatin significantly reduced LDL-cholesterol and apoliprotein B levels compared with baseline or placebo (all *P*<0.001) for all doses
- Atorvastatin significantly increased fasting plasma insulin and HbA<sub>1c</sub> levels, and decreased insulin sensitivity, when compared with baseline or placebo, for all doses (all *P*≤0.03).
- While inducing beneficial reductions in LDL-cholesterol and apolipoprotein B, atorvastatin treatment resulted in significant increases in insulin resistance and increased ambient glycaemia among a population with hypercholesterolemic.

Koh KK, Quon MJ, Han SH et al (2010) Atorvastatin causes insulin resistance and increases ambient glycemia in hypercholesterolemic patients. *J Am Coll Cardiol* **23**: 1209–16

#### **Clinical** *DIGEST 3*

## AMERICAN JOURNAL OF CARDIOLOGY

# Low HbA<sub>1c</sub> improves outcomes in coronary revascularisation

Readability / / /
Applicability to practice / / /
WOW! factor / / /

This Japanese study explored the association between preoperative HbA<sub>1c</sub> levels and CV outcomes in 3571 people (1504 with T2D treated with antidiabetes drugs) undergoing coronary revascularisation.

People with T2D with HbA $_{1c}$  levels <6% (<42 mmol/mol) had the lowest rate of freedom from major adverse CV events (MACEs).

HbA<sub>1c</sub> levels ≥6% (≥42 mmol/mol) but <7% (<53 mmol/mol) were associated with the lowest MACE hazard ratio compared with people without T2D.

It was concluded that the lowest risk of MACE was incurred by people with T2D undergoing first coronary revascularisation with an HbA<sub>tc</sub> level of 6–7% (42–53 mmol/mol).

Ehara N, Morimoto T, Furukawa Y et al (2010) Effect of baseline glycemic level on long-term cardiovascular outcomes after coronary revascularization therapy in patients with type 2 diabetes mellitus treated with hypoglycemic agents. *Am J Cardiol* **105**: 960–6

#### CIRCULATION

# Antiatherosclerotic effect of rosiglitazone not significant

This 18-month study assessed the progression of atherosclerosis in 672 people with T2D treated with rosiglitazone or glipizide who had at least one atherosclerotic plaque with 10–50% luminal narrowing in a coronary artery that had not undergone intervention.

Change in percent atheroma volume in the longest and least angulated epicardial coronary artery was the primary outcome investigated.

Rosiglitazone did not significantly reduce the percent atheroma volume compared with glipizide (-0.64%; 95% confidence interval [CI], -1.46 to 0.17; *P*=0.12) and no significant difference between groups was observed for the change in total atheroma volume within the most diseased 10 mm segment at baseline(-1.7 mm³; 95% CI, -3.9 to 0.5; *P*=0.13).

Among people with T2D and coronary atherosclerosis, the authors concluded that rosiglitazone therapy did not significantly slow the progression of atherosclerosis more than treatment with glipizide.

Gerstein HC, Ratner RE, Cannon CP et al (2010) Effect of rosiglitazone on progression of coronary atherosclerosis in patients with type 2 diabetes mellitus and coronary artery disease: The assessment on the prevention of progression by rosiglitazone on atherosclerosis in diabetes patients with cardiovascular history trial. *Circulation* **121**: 1176–87

#### AMERICAN JOURNAL OF CARDIOLOGY

### Clopidogrel reduces vascular damage

Elevated levels of circulating endothelial cells (CECs), an indicator of vascular injury, is known to be common among people with T2D.

Blood specimens were assayed for

CECs from nine people with T2D and endothelial progenitor cells analysed for expression of phosphorylated

Akt and phosphorylated adenosine monophosphate kinase (PAMK). Subjects were then administered with clopidogrel (75 mg/day for 30 days).

Participants had reduced CEC levels following treatment with clopidogrel (mean 10±4 cells/mL; *P*<0.001).

There was a significant increase in the expression of both phosphorylated Akt and PAMK ( $P \le 0.05$ ) by study end.

These results suggest that clopidogrel can promote improved vascular function in people with T2D.

McClung JA, Kruger AL, Ferraris A et al (2010) Usefulness of clopidogrel to protect against diabetes-induced vascular damage. *Am J Cardiol* **105**: 1014–18