Cardiovascular journals

AMERICAN JOURNAL OF CARDIOLOGY

DPP-4 inhibitors may decrease CV risk in long term

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

1 Although individuals with T2D have a high risk for cardiovascular (CV) events, some oral treatments for T2D generally do not improve CV outcomes despite lowering blood glucose levels.

2 Dipeptidyl peptidase-4 (DPP-4) inhibitors are a novel treatment for T2D; they are well tolerated with relatively few side effects and a low incidence of hypoglycaemia.

3 In this meta-analysis the authors studied the effect of DPP-4 inhibitors on long-term CV events by analysing data from randomised controlled trials of individuals with T2D treated with DPP-4 inhibitor monotherapy versus other oral treatments or placebo.

4 The study comprised 18 trials including 4998 participants randomised to a DPP-4 inhibitor and 3546 to a comparator for a median of 46.4 weeks.

5 The use of DPP-4 inhibitors was associated with a lower risk of adverse CV events (relative risk [RR], 0.48; 95% confidence interval [CI], 0.31–0.75; *P*=0.001) and a lower risk of non-fatal myocardial infarction or acute coronary syndrome (RR, 0.40; 95% CI, 0.18–0.88; *P*=0.02) compared with other oral hypoglycaemic agents or placebo.

6 This meta-analysis is sufficiently powered to demonstrate that the novel DPP-4 inhibitors appear to decrease the risk of CV events.

Patil HR, Al Badarin FJ, Al Shami HA et al (2012) Meta-analysis of effect of dipeptidyl peptidase-4 inhibitors on cardiovascular risk in type 2 diabetes mellitus. *Am J Cardiol* **110**: 826–33

Initial results indicate that the novel DPP-4 inhibitors have potential cardiovascular benefits

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Dipeptidyl peptidase-4 (DPP-4) inhibitors are a relatively new class of blood-glucose-lowering therapy for people with T2D, with potential benefits in relation to both body weight and the risks of hypoglycaemia derived from extensive, albeit relatively short-term, clinical trial data. Consequently, these agents are increasingly used in routine clinical practice and are endorsed by both national and international guidelines.

Cardiovascular (CV) disease represents the major cause of morbidity and mortality in T2D. Multiple studies have failed to demonstrate any CV outcome benefits with individual blood-glucose-lowering therapies, and the long-term CV effects of DPP-4 inhibitors are the focus of numerous large-scale outcome studies.

The objective of this meta-analysis was to analyse all relevant clinical trials comparing DPP-4 inhibitors with either another blood-glucose-lowering agent or placebo. Eighteen randomised trials met the criteria for this meta-analysis, comprising 4998 people who received a DPP-4 inhibitor and 3546 a comparator, with a median duration of therapy of 46.4 weeks. The relative risk (RR) of any adverse CV event with any DPP-4 inhibitor was 0.48 (95% confidence interval [CI], 0.31–0.75; *P*=0.001), while the RR for non-fatal myocardial infarction (MI) and acute coronary syndrome was 0.40 (95% CI, 0.18–0.88; *P*=0.02). None of the individual studies included in this meta-analysis were powered to specifically assess the CV effects of these agents; this analysis is thus an important data source as it is the first adequately powered study to enable an evaluation of the potential CV effects of DPP-4 inhibitors to be made.

The results appear to suggest a potential CV benefit for DPP-4 inhibitors as manifest by a 52% RR reduction in CV events and a 60% reduction in MI or acute coronary syndrome. These benefits were seen in comparison with other blood-glucose-lowering therapies, but when compared with placebo no difference was detected. This may reflect a lack of statistical power, with only 23% of subjects receiving placebo, or alternatively may relate to possible adverse CV effects of alternative blood-glucose-lowering therapies. The reduction in CV events appeared to be present for all agents within the class, including sitagliptin, vildagliptin, saxagliptin, linagliptin and alogliptin.

It is important to remember that this analysis has several limitations: it is based on relatively short-term studies that were inadequately powered to assess CV safety; there is a lack of patient-level data; and not all DPP-4 inhibitor studies reported CV outcomes. Consequently, while these data appear encouraging from the perspective of potential CV benefits of DPP-4 inhibitors, the results of the multiple, ongoing clinical trials specifically evaluating this issue are required before making any final judgment as to the true CV effects of DPP-4 inhibitors.

AMERICAN JOURNAL OF CARDIOLOGY

Niacin increases glycaemia but reduces CV events

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

1 Niacin reduces the progression of atherosclerosis and the incidence of cardiovascular (CV) events, but is known to increase glycaemia in people with diabetes.

2 The authors examined the effects of niacin on glucose levels, coronary stenosis progression and clinical events in 407 people without diabetes enrolled in lipid trials.

3 The use of niacin for 3 years in participants with normal baseline glucose levels was associated with increased glycaemia and risk of developing impaired fasting glucose, but not diabetes; however, niacin was associated with a significantly reduced incidence of coronary stenosis progression and major CV events.

Phan BA, Muñoz L, Shadzi P et al (2012) Effects of niacin on glucose levels, coronary stenosis progression and clinical events in subjects with normal baseline glucose levels. *Am J Cardiol* **111**: 352–5

"Characteristics such as age, gender, education, physical activity, smoking, central obesity and comorbidities were significantly associated with health-related quality of life in individuals with coronary heart disease."

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Atorvastatin 80 mg reduces CV events across NOD risk

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

1 Although it is known that statin therapy reduces cardiovascular (CV) risk, some studies have shown that statins can increase the risk of new-onset diabetes (NOD) compared with placebo.

2 The reduction in CV risk compared with risk of NOD has not been evaluated in individuals at differing levels of diabetes risk.

3 The study objective was to evaluate the incidence of NOD and CV events according to baseline risk factors for diabetes within two large secondary prevention trials with atorvastatin.

4 The analysis comprised 15 056 people with CV disease but without diabetes at baseline: 7595 who had been randomised to atorvastatin 10 mg or 80 mg daily and followed for a median of 4.9 years; and 7461 who had been randomised to simvastatin 20–40 mg daily or atorvastatin 80 mg daily and followed for a median of 4.8 years.

5 From a previous report, the four factors identified that independently predict NOD are a fasting blood glucose >100 mg/dL (5.6 mmol/L), fasting triglycerides >150 mg/dL (1.7 mmol/L), BMI >30 kg/m^2 and a history of hypertension.

6 Compared with lower-dose statin therapy, atorvastatin 80 mg/day did not increase the incidence of NOD in individuals with 0–1 NOD risk factors, but did increase NOD incidence by 24% in those with 2–4 NOD risk factors.

7 Compared with low-dose statin, atorvastatin 80 mg reduced the number of CV events in individuals at low and high risk for diabetes.

Waters DD, Ho JE, Boekholdt SM et al (2013) Cardiovascular event reduction versus new-onset diabetes during atorvastatin therapy. *J Am Coll Cardiol* **61**: 148–52

INTERNATIONAL JOURNAL OF CARDIOLOGY

HRQoL in people with CHD differs between countries

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

1 People with coronary heart disease (CHD) are known to have an impaired health-related quality of life (HRQoL).

2 In this study the authors examined the relationship between individuals' cardiovascular profile and their HRQoL across 22 European countries using data from the EUROASPIRE III survey.

3 In total, 8734 people with CHD were interviewed and examined; quality of life was assessed using two questionnaires (the EuroQoL-5D and the 12-item short-form health survey).

4 HRQoL scores were found to significantly differ between countries, even after adjustments (P<0.001); individuals with CHD residing in Eastern European countries were more likely to have lower HRQoL scores.

5 Characteristics such as age, gender, education, physical activity, smoking, central obesity and comorbidities were significantly associated with HRQoL in individuals with CHD.

De Smedt D, Clays E, Annemans L et al (2012) Health-related quality of life in coronary patients and its association with their cardiovascular risk profile. *Int J Cardiol* 29 Nov [Epub ahead of print]

EUROPEAN HEART JOURNAL

Glycaemic variability does not worsen prognosis after AMI

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

1 As the prognosis after acute myocardial infarction (AMI) is worse for individuals with diabetes, the authors examined whether this was caused by glycaemic variability.

2 The study included 578 individuals with T2D who had their glucose levels measured hourly during insulin–glucose infusion for the first 48 hours of admission for AMI.

3 In unadjusted analyses, glycaemic variability did not differ between individuals who died during the 1-year follow-up compared with survivors.

4 After adjustments, the 1-year risk for death, reinfarction or stroke did not relate to glycaemic variability after AMI.

Mellbin LG, Malmberg K, Rydén L et al (2012) The relationship between glycaemic variability and cardiovascular complications in patients with acute myocardial infarction and type 2 diabetes. *Eur Heart J* 9 Nov [Epub ahead of print]

AMERICAN JOURNAL OF CARDIOLOGY

Incidence of new diabetes is high in people with CVD

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

1 Although it is known that diabetes is a risk factor for the development of cardiovascular disease (CVD), less is known about the real incidence of new cases of diabetes in people with CVD.

2 In total, 338 individuals with CVD and without known diabetes underwent oral glucose tolerance testing (OGTT).

3 Of the initial cohort, OGTT identified 115 with normal glycaemia, 143 with pre-diabetes and 80 with unknown diabetes.

4 After a mean 3.13 years' follow-up, 191 survivors were reassessed with OGTT; 25 new cases of diabetes were identified.

5 The overall incidence of diabetes was 43.6 cases per 1000 person-years, but was significantly higher in the initial prediabetes group (70.5 cases per 1000 person-years).

de la Hera JM, García-Ruiz JM, Martínez-Camblor P et al (2012) Real incidence of diabetes mellitus in a coronary disease population. *Am J Cardiol* 17 Nov [Epub ahead of print]