Cardiovascular journals

EUROPEAN HEART JOURNAL

Most SUs increase mortality compared with metformin

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

1 Although metformin is generally recognised as the first-line treatment strategy for people with T2D, sulphonylureas (SUs) are also widely used.

2 Few randomised studies have examined the effect of long-term SU monotherapy on mortality outcomes, and the long-term cardiovascular (CV) safety and efficacy of metformin compared with different SU monotherapies remains unclear.

3 The authors performed a nationwide study to determine the mortality outcomes and CV risk related to different SU monotherapies compared with metformin in people with T2D with high and low CV risk, as defined by previous myocardial infarction (MI).

4 The study cohort comprised 107 806 Danish adults on SU monotherapy or metformin for T2D; 9607 participants had a history of MI.

5 SU monotherapy included glimepiride, gliclazide, glibenclamide, glipizide, tolbutamide and repaglinide; participants were followed-up for up to 9 years (median 3.3 years).

6 Analyses showed an increase in all-cause mortality associated with glimepiride, glibenclamide, glipizide and tolbutamide compared with metformin in participants with and without a history of MI; results were similar for CV mortality.

7 Most SU monotherapy was found to increase mortality and CV risk compared with metformin; gliclazide and repaglinide, however, gave similar results to metformin, with a lower risk than other SUs.

Schramm TK, Gislason GH, Vaag A et al (2011) Mortality and cardiovascular risk associated with different insulin secretagogues compared with metformin in type 2 diabetes, with or without a previous myocardial infarction: a nationwide study. *Eur Heart J* **32**: 1900–8

Sulphonylurea monotherapy: Increased mortality and CV risk when compared with metformin?

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Metformin is recommended as first-line therapy for managing people with type 2 diabetes; sulphonylureas (SUs) are recommended as second-line therapy (NICE, 2009). The majority of SU prescriptions in the UK are for gliclazide, and there is now good evidence to support this, especially in light of recent pharmacy advice and pressure in some PCTs. The main cost issue is that gliclazide modified-release is more expensive than glibenclamide or glimepiride if a once-daily SU is desired.

Schramm et al (2011; summarised alongside) researched the Danish Registry of Medicinal Product Statistics to investigate whether there is a mortality or cardiovascular disease (CVD) benefit associated with SUs in comparison with metformin use as first-line therapy in type 2 diabetes. A total of 107 806 individuals were studied for just over 2 years, 9607 of whom had a previous myocardial infarction (MI). All-cause mortality, CVD mortality and CVD events was the composite outcome measure.

Compared with metformin, the hazard ratio (HR) for SU use was found to be significantly increased both in those with or without previous MI: glimepiride, 1.32 and 1.30; glibenclamide, 1.19 and 1.47; glipizide, 1.27 and 1.53; and tolbutamide, 1.28 and 1.47, respectively. Gliclazide was not associated with a significant difference from metformin in those with or without a previous MI.

The reason is difficult to ascertain with a great deal of certainty, but it is hypothesised that SUs such as glibenclamide, by binding to SU 2A receptors in the myocardium, are associated with reduced ischaemic pre-conditioning. This may help to explain the increased CVD events in the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial, which used SUs other than gliclazide (ACCORD Study Group et al, 2008). In the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation) study, which used gliclazide, there was a small but significant reduction in CVD events with tight glycaemic control using gliclazide (ADVANCE Collaborative Group et al, 2008).

Action to Control Cardiovascular Risk in Diabetes Study Group, Gerstein HC, Miller ME et al (2008) Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* **358**: 2545–59

ADVANCE Collaborative Group, Patel A, MacMahon S et al (2008) Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med* **358**: 2560–72

NICE (2009) *Type 2 Diabetes: The Management of Type 2 Diabetes.* NICE, London

AMERICAN JOURNAL OF CARDIOLOGY

Physical activity reduces the risk of CVD mortality

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

1 Physical activity (PA) is known to improve metabolic risk factors linked with cardiovascular disease (CVD) and to reduce CVD mortality.

2 The authors examined the extent to which metabolic risk factors mediate the association between PA and CVD mortality in 10 261 adults from the Third National Health and Nutrition Examination Survey.

3 Data were taken from the public access mortality linkage file with follow-up for 13.4±3.9 years; PA was assessed by questionnaire and metabolic risk factors classified using clinical thresholds.

4 Most participants engaged in light (42.1%) or moderate/vigorous (37.5%) PA, which were associated with reduced CVD mortality. This relationship was found to be independent of the metabolic risk factors that were suggested to mediate this association.

5 The authors concluded that PA protected against CVD mortality irrespective of the metabolic profile, and thus should be recommended for its protective effects.

Reddigan JI, Ardern CI, Riddell MC, Kuk JL (2011) Relation of physical activity to cardiovascular disease mortality and the influence of cardiometabolic risk factors. *Am J Cardiol* [Epub ahead of print]

"The large sample size and differing cohorts support the evidence that aspirin is effective at decreasing cardiovascular risk."

AMERICAN JOURNAL OF CARDIOLOGY

PCI for CTOs reduce mortality in diabetes

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

1 To determine the effect of diabetes on long-term outcomes, the authors compared results after percutaneous coronary intervention (PCI) for chronic total occlusions (CTOs) in 1742 participants, 395 with diabetes.

2 Comparisons included successful versus failed PCI for CTOs and the use of drug-eluding stents (DES) versus bare-metal stents (BMS) in participants with and without diabetes.

3 PCI for CTOs was similarly successful in participants with versus those without diabetes; stents were implanted in 96.4% of participants with diabetes (76.2% DES vs 23.8% BMS) and in 94.0% of those without diabetes (61.4% DES vs 38.6% BMS).

4 PCI for CTOs in people with diabetes was linked with a reduction in mortality and the need for coronary artery bypass grafting. DESs were linked with a reduction in revascularisation irrespective of diabetes status.

Claessen BE, Dangas GD, Godino C et al (2011) Long-term clinical outcomes of percutaneous coronary intervention for chronic total occlusions in patients with *vs* without diabetes mellitus. *Am J Cardiol* **108**: 924–31

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

IFG does not increase risk for CV events

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

1 People with impaired fasting glucose (IFG) are at increased risk of developing T2D; however, the relationship between IFG and cardiovascular (CV) events remains unclear.

2 To determine whether IFG affects CV risk, 6753 people were recruited in the Multi-Ethnic Study of Atherosclerosis; 840 (12.4%) had T2D, 940 (13.9%) had IFG and 4973 (73.6%) had normal fasting glucose (NFG) at baseline.

3 Over 7.5 years of follow-up there were 418 adjudicated CV events: 105 in the T2D group, 72 in the IFG group, and 241 in the NFG group.

4 Having IFG was associated with an increased risk of T2D; intervention for people with IFG will reduce this risk.

5 The authors concluded that IFG was not an independent risk factor for CV events.

Yeboah J, Bertoni AG, Herrington DM et al (2011) Impaired fasting glucose and the risk of incident diabetes mellitus and cardiovascular events in an adult population: MESA (Multi-Ethnic Study of Atherosclerosis). *J Am Coll Cardiol* **58**: 140–6

AMERICAN JOURNAL OF CARDIOLOGY

Aspirin effective at preventing CV events

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

1 The authors present a meta-analysis of nine studies that examined the effectiveness of aspirin (acetylsalicylic acid) in the primary prevention of cardiovascular (CV) events.

2 The combined data comprises 50 868 participants who were treated with aspirin and 49 170 who received placebo or control.

3 Participants receiving aspirin had a significantly decreased risk of non-fatal myocardial infarction (P=0.042) and total CV events (P=0.001).

4 Taking aspirin had no significant effect on total coronary heart disease, stroke, CV and all-cause mortality.

5 The large sample size and differing cohorts support the evidence that aspirin is effective at decreasing CV risk when compared with none or placebo.

6 It was concluded that the benefits of aspirin for CV prevention must be weighed up against any risks on an individual basis.

Bartolucci AA, Tendera M, Howard G (2011) Meta-analysis of multiple primary prevention trials of cardiovascular events using aspirin. *Am J Cardiol* **107**: 1796–1801

AMERICAN JOURNAL OF CARDIOLOGY

ACE inhibitors reduce diabetes risk caused by beta-blockers

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

1 The use of beta-blockers has been linked with an increased risk for developing new-onset diabetes (NOD); however, the use of angiotensin-converting enzyme (ACE) inhibitors might reduce this risk.

2 This study aimed to determine the effect of beta-blockers on risk for NOD in 8290 people with stable coronary artery disease (CAD) recruited to the PEACE (Prevention of Events with Angiotensin-Converting Enzyme Inhibition) trial, and whether this risk was attenuated by ACE inhibitors.

3 In total, 6910 people with stable CAD were randomised to receive either the ACE inhibitor trandolapril (n=3436) or placebo (n=3474), and were followed-up for 4.8 years; 1380 people were excluded as they had diabetes at baseline.

4 Of those participants taking beta-blockers, 2057 were in the ACE-inhibitor group and 2090 were in the placebo group.

5 In total, 733 people developed NOD; there was a significant link between beta-blockers and ACE inhibition with respect to NOD (P=0.028).

6 People randomised to placebo were at increased risk of developing NOD after adjustments (hazard ratio [HR], 1.63; 95% confidence interval [CI], 1.29–2.05; P<0.001); randomisation to the ACE-inhibitor group resulted in a reduced risk of developing NOD (HR, 1.11; 95% CI, 0.87–1.42; P=0.39).

7 The authors concluded that using ACE inhibitors may attenuate the risk of NOD in people with stable CAD taking beta-blockers.

Vardeny O, Uno H, Braunwald E et al (2011) Opposing effects of β-blockers and angiotensin-converting enzyme inhibitors on development of new-onset diabetes mellitus in patients with stable coronary artery disease. *Am J Cardiol* **107**: 1705–9

AMERICAN JOURNAL OF CARDIOLOGY

Vitamin D deficiency present in acute MI

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

1 Although there is a link between vitamin D deficiency and cardiovascular disease (CVD), the prevalence of vitamin D deficiency in people with acute myocardial infarction (MI) is unknown.

2 This study comprised 239 adults with biomarker evidence of MI and supporting evidence of acute MI who presented within 24 hours of symptom onset; participants were enrolled in a prospective MI registry from 1 June to 31 December 2008.

3 Levels of 25-hydroxyvitamin D (25[OH]D) were assessed at baseline; normal levels of 25(OH)D are considered to be ≥30 ng/mL, insufficient levels of 25(OH)D are 21–29 ng/mL and deficient levels of 25(OH)D are ≤20 ng/mL.

4 Results showed that 229 participants (96%) had suboptimal levels of 25(OH)D at baseline; 179 (75%) had deficient 25(OH)D levels of ≤20 ng/ml and 50 (21%) had insufficient 25(OH)D levels of 21–29 ng/ml.

5 Deficient levels of 25(OH)D were more commonly seen in non-caucasians, those with diabetes, those who were more inactive and those with higher parathyroid hormone levels (45.3 vs 32.7 pg/mL; $P=0.029$) and BMI (31.2 vs 29.0 kg/m^2; $P=0.025$).

6 The high prevalence of vitamin D deficiency or insufficiency supports studies linking CVD and many of its risk factors with 25(OH)D deficiency.

7 It was concluded that studies are needed to determine whether normalising vitamin D levels in people with acute MI will improve CV health and prognosis.

Lee JH, Gadi R, Spertus JA et al (2011) Prevalence of vitamin D deficiency in patients with acute myocardial infarction. *Am J Cardiol* **107**: 1636–8

AMERICAN HEART JOURNAL

Hospital care does not affect outcome in diabetes with HF

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

1 Although morbidity and mortality is high in people with heart failure (HF) and comorbid diabetes, it is unknown whether outcome is associated with quality of care in hospital.

2 To determine the effect of hospital care on outcome, the study cohort comprised 133 971 admissions with HF from 431 hospitals between January 2005 and January 2010.

3 In total, 61 318 (45.8%) participants had reduced left ventricular ejection fraction (LVEF) and 63 888 (47.7%) had preserved LVEF.

4 There were 54 352 participants with diabetes hospitalised for HF (40.6%): 23 811 had reduced LVEF (39%); and 27 287 had preserved LVEF (43%).

5 There were no significant differences in receiving the composite of angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) and beta-blockers, ACEI/ARB, evidence-based beta-blockers and hydralazine/nitrates between participants with and without diabetes.

6 Those admitted with diabetes were less likely to receive counselling to stop smoking, to achieve blood pressure control and to attain the all-or-none composite measure.

7 Participants with diabetes were more likely to receive an aldosterone antagonist for reduced LVEF, a lipid-lowering agent and influenza vaccination.

8 Participants with diabetes had longer hospital stays but there were no significant differences in rates of in-hospital mortality between groups.

Kapoor JR, Fonarow GC, Zhao X et al (2011) Diabetes, quality of care and in-hospital outcomes in patients hospitalised with heart failure. *Am Heart J* **162**: 480–6

HEART

OGTT best detects diabetes in ACS

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

1 People with acute coronary syndrome (ACS) often have elevated plasma glucose levels on admission (APG); an elevated APG can be the first indication of diabetes.

2 This study sought to determine the prevalence of previously undetected diabetes and to compare different ways to diagnose diabetes in 130 people with ACS and elevated APG from the BIOMArCS 2 (Biomarker Study to Identify the Acute Risk of a Coronary Syndrome) glucose trial.

3 Of the participants, 109 underwent an oral glucose tolerance test (OGTT) before discharge and 13 people had pre-existing diabetes.

4 Admission HbA_{1c}, fasting plasma glucose (FPG) and APG were compared with the OGTT result to determine the best diagnostic method for detecting diabetes.

5 OGTT results detected previously undiagnosed diabetes in 38 participants (35%) and impaired glucose metabolism in 48 participants (44%); only 23 participants (21%) had normal glucose metabolism.

6 Using an FPG of ≥7.0 mmol/L and an HbA_{1c} level of ≥6.5% (≥48 mmol/mol) as diagnostic cut-offs detected only 14 and 11 of the 38 people with undiagnosed diabetes, respectively; it was not possible to determine an APG cut-off value to predict undiagnosed diabetes.

7 An OGTT pre-discharge was the most sensitive method for detecting previously undiagnosed diabetes and impaired glucose metabolism; the authors recommended that this should become standard care in people admitted with ACS, especially with elevated APG.

de Mulder M, Oemrawsingh RM, Stam F et al (2011) Comparison of diagnostic criteria to detect undiagnosed diabetes in hyperglycaemic patients with acute coronary syndrome. *Heart* [Epub ahead of print]

"The high prevalence of vitamin D deficiency or insufficiency supports studies linking cardiovascular disease and many of its risk factors with 25(OH)D deficiency."