Diabetes journals

DIABETES CARE

Metformin improves outcomes in people with heart failure and type 2 diabetes

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

1 Treatment with metformin is contraindicated in people with heart failure, based on concerns that it may lead to lactic acidosis.

2 The authors explain, however, that alternatives to metformin for the treatment of type 2 diabetes in people with heart failure are not ideal.

3 The authors used the Saskatchewan Health database to identify 1833 people with heart failure in order to compare clinical outcomes with metformin (n=208), sulphonylurea (n=773) and their combination (n=852).

4 Differences in all-cause mortality, all-cause hospitalisations and their combination were assessed using a mulitvariate Cox proportional hazards model.

5 Compared with people on sulphonylurea alone, there were significantly fewer deaths in those on metformin alone (hazard ratio [HR], 0.70; 95% confidence interval [CI], 0.54–0.91) or the combination (HR, 0.61; 95% CI, 0.52–0.72).

6 There were also significant reductions in the combination of deaths and hospitalisations, relative to sulphonylurea monotherapy, for metformin monotherapy (HR, 0.83; 95% CI, 0.70–0.99) and the combination (HR, 0.86; 95% CI, 0.77–0.96).

Eurich DT, Majumdar SR, McAlister FA, Tsuyuki RT, Johnson JA (2005) Improved clinical outcomes associated with metformin in patients with diabetes and heart failure. *Diabetes Care* **28**(10): 2345–51

Metformin may be safe in people with heart failure

Marc Evans, Consultant Physician, Llandough Hospital, Cardiff

Heart failure is common in people with type 2 diabetes and diabetes is associated with poorer outcomes in individuals with heart failure (De Groote et al, 2004). Based on data from the UK Prospective Diabetes Study Group (1998), in which metformin therapy was associated with cardiovascular outcome benefits, metformin is now accepted as first-line oral hypoglycaemic therapy in type 2 diabetes. However, metformin has been considered contraindicated in people with heart failure because of concerns over lactic acidosis.

Using the Saskatchewan Health databases, Eurich et al (see left) assessed the association between metformin and clinical outcomes in people with heart failure and type 2 diabetes. Metformin therapy either alone or in combination with a sulphonylurea was associated with lower all-cause mortality rates compared with sulphonylurea therapy alone, even after adjusting for confounding variables. Furthermore, metformin was not associated with an increase in hospitalisations, suggesting that metformin therapy is safe in this vulnerable population. Importantly, no cases of metabolic acidosis were noted during the follow-up period.

This is an observational study and, as such, cannot conclusively prove that metformin therapy in people with heart failure results in improved clinical outcomes; however, it does raise an intriguing hypothesis that warrants further evaluation in a clinical trial setting. The beneficial effects of metformin appeared to be independent of glycaemia and were not confounded by factors shown to be prognostic in heart failure. There was no evidence of any increase in morbidity associated with metformin therapy; indeed, fewer hospitalisations occurred compared with sulphonylurea, suggesting that although it is contraindicated in this population, metformin may not only be safe but also potentially result in outcome benefits. This challenges the current dogma that metformin is unsafe in people with heart failure.

De Groote P, Lamblin N, Mouquet F, Plichon D, McFadden E, Van Belle E, Bauters C (2004) Impact of diabetes mellitus on long-term survival in patients with congestive heart failure. *European Heart Journal* **25**(8): 656–62

UK Prospective Diabetes Study (UKPDS) Group (1998) Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet* **352**(9131): 854–65

DIABETES CARE

Risk reduction with statins independent of diagnosis of metabolic syndrome

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

1 Study-defined criteria for the metabolic syndrome were applied to 3038 patients from the Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) trial who were admitted to hospital wih unstable angina or non-Q wave acute myocardial infarction.

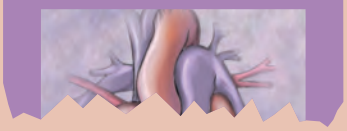
2 The primary end point assessed was a composite of death, myocardial infarction, cardiac arrest or recurrent unstable myocardial ischaemia.

3 This end point had an incidence of 19.2% in patients with the metabolic syndrome (n=1161) and 14.3% in those without (n=1877).

4 The relative risk reduction with atorvastatin 80 mg daily was similar for patients with the metabolic syndrome and those without; across all patients, though, there was an absolute risk reduction of 2.6%.

Schwartz GG, Olsson AG, Szarek M, Sasiela WJ (2005) Relation of characteristics of metabolic syndrome to short-term prognosis and effects of intensive statin therapy after acute coronary syndrome: an analysis of the Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) trial. *Diabetes Care* **28**(10): 2508–13

DIABETES CARE



Higher prevalence of metabolic syndrome with new IDF criteria

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

1 The International Diabetes Federation (IDF) recently revealed a new approach to defining the metabolic syndrome, one that stresses central adiposity based on ethnic group-specific cut-offs.

2 This study estimated the incidence of the metabolic syndrome among US adults based on this definition, and compared it with the incidence estimated using the National Cholesterol Education Program (NCEP) Adult Treatment Panel III definition.

3 The analyses included 3601 people from the National Health and Nutrition Examination Survey (1999–2002).

4 Using the NCEP definition, the prevalence (± SE) of the metabolic syndrome was found to be 34.5 ± 0.9 % across all participants, 33.7 ± 1.6 % in men and 35.4 ± 1.2 % in women.

5 With the new IDF definition, these prevalence estimates were higher: 39.0 ± 1.1 % across all participants, 39.9 ± 1.7 % in men and 38.1 ± 1.2 % in women.

6 The differences held across demographic groups, being particularly pronounced in Mexican–American men.

Ford ES (2005) Prevalence of the metabolic syndrome defined by the International Diabetes Federation among adults in the U.S. *Diabetes Care* **28**(11): 2745–9

DIABETES CARE

Elevated urinary albumin excretion predicts onset of type 2 diabetes

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

1 Data from 5654 participants in the Prevention of Renal and Vascular End Stage Disease study were used to assess the relationship between urinary albumin excretion (UAE) and the development of type 2 diabetes, with regard to C-reactive protein (CRP) and the metabolic syndrome.

2 In a model controlled for age, sex, number of metabolic syndrome components and known risk factors for type 2 diabetes, UAE was positively related to the onset of type 2 diabetes (odds ratio [OR], 1.53; 95 % confidence interval [CI], 1.25–1.88; $P<0.001$).

3 For tertiles based on CRP levels, the odds ratios were 2.2 (95 % CI, 1.47–3.3), 1.33 (95 % CI, 0.96–1.84) and 1.04 (95 % CI, 0.83–1.31), from lowest to highest tertiles, respectively; this meant that UAE's predictive value was modified by CRP levels.

Brantsma AH, Bakker SJ, Hillege HL et al (2005) Urinary albumin excretion and its relation with C-reactive protein and the metabolic syndrome in the prediction of type 2 diabetes. *Diabetes Care* **28**(10): 2525–30

DIABETIC MEDICINE

Serum GGT linked to metabolic syndrome components

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

1 Several studies have shown serum γ-glutamyltransferase (GGT) to be associated with components of the metabolic syndrome, but they have typically involved few participants or had insufficient exclusion criteria.

2 This medical record investigation (n=29 959) had comprehensive exclusion criteria.

3 Within the normal range of serum GGT, higher concentrations were significantly related to greater frequencies of diabetes, impaired fasting glucose, obesity and dyslipidaemia in both men and women.

Kim DJ, Noh JH, Cho NH et al (2005) Serum gamma-glutamyltransferase within its normal concentration range is related to the presence of diabetes and cardiovascular risk factors. *Diabetic Medicine* **22**(9): 1134–40

DIABETOLOGIA

TV watching related to metabolic syndrome incidence

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

1 There is a lack of research into the influence of sedentary behaviour and physical activity on components of the metabolic syndrome, with the exception of obesity.

2 In this study, 6241 Australian adults without diabetes self-reported TV watching and physical activity during one week.

3 The metabolic syndrome was defined by the World Health Organization's 1999 criteria.

4 Compared with watching TV for no more than 7 hours, watching it for over 14 hours yielded odds ratios for having the metabolic syndrome in women and men of 2.07 (95 % confidence interval [CI], 1.49–2.88) and 1.48 (not significant), respectively.

5 Compared with doing physical activity for under 2.5 hours, doing it for at least 2.5 hours yielded odds ratios for having the metabolic syndrome in women and men of 0.53 (95 % CI, 0.38–0.74) and 0.72 (95 % CI, 0.58–0.90), respectively.

Dunstan DW, Salmon J, Owen N et al (2005) Associations of TV viewing and physical activity with the metabolic syndrome in Australian adults. *Diabetologia* **48**(11): 2254–61

'Within the normal range of serum γ-glutamyltransferase, higher concentrations were significantly related to greater frequencies of diabetes.'

'Urinary albumin excretion was positively related to the onset of type 2 diabetes.'

DIABETOLOGIA

Dysglycaemia leads to CV events, renal disease and death

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

1 As part of the Heart Outcomes Prevention Evaluation (HOPE) study, this prospective, epidemiological analysis explored the effect on cardiovascular (CV) and renal events of dysglycaemia (assessed by glycated haemoglobin in 3529 people and fasting pasma glucose [FPG] in 2950 people).

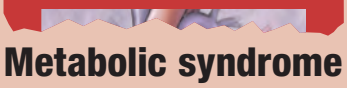
2 A 1-percentage-point increase in glycated haemoglobin from baseline predicted future CV events (P=0.014), overt nephropathy (P<0.0001) and death (P=0.0004).

3 A 1 mmol/l increase in FPG also predicted future CV events (P<0.0001), overt nephropathy (P<0.0001) and death (P=0.0007).

4 These findings link hyperglycaemia to CV outcomes and thus add to evidence suggesting that glucose lowering may reduce CV risk.

Gerstein HC, Pogue J, Mann JF et al (2005) The relationship between dysglycaemia and cardiovascular and renal risk in diabetic and non-diabetic participants in the HOPE study: a prospective epidemiological analysis. *Diabetologia* **48**(9): 1749–55

DIABETES



Metabolic syndrome predicts CVD independent of IR

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

1 It is unknown if the metabolic syndrome's effect on cardiovascular disease (CVD) is independent of that of insulin resistance (IR).

2 This investigation included 2898 participants of the Framingham Offspring Study, none of whom had CVD or diabetes at baseline.

3 The metabolic syndrome was defined using National Cholesterol Education Progam Adult Treatment Panel III criteria.

4 IR was measured by the Homeostasis Model Assessment (HOMA-IR) and an insulin sensitivity index ($ISI_{0,120}$).

5 Models for 7-year CVD risk revealed associations with the metabolic syndrome, HOMA-IR and $ISI_{0,120}$.

6 In a model with $ISI_{0,120}$ and the metabolic syndrome, both were independently linked to CVD risk, while in a model that included HOMA-IR and the metabolic syndrome, there was only an independent association for the latter.

Rutter MK, Meigs JB, Sullivan LM, D'Agostino RB Sr, Wilson PW (2005) Insulin resistance, the metabolic syndrome, and incident cardiovascular events in the framingham offspring study. *Diabetes* **54**(11): 3252–7

DIABETIC MEDICINE

Sex-specific effect of diabetes on ACS identified

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

1 This study explored clinical presentation, in-hospital course and short-term prognosis in people with diabetes and acute coronary syndromes (ACS).

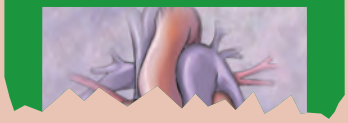
2 Women (n=2809) and men (n=6488) discharged with a diagnosis of ACS were enrolled into the Euro Heart Survey ACS.

3 After adjustment for confounding factors, the presence of diabetes in women with ACS was associated with a greater likelihood of presenting with ST elevation (odds ratio [OR], 1.46; 95% confidence interval [CI], 1.20–1.78), developing Q-wave myocardial infarction (OR, 1.61; 95% CI, 1.30–1.99) and dying in hospital (OR, 2.13; 95% CI, 1.39–3.26).

4 No such differences were found in men with ACS.

Dotevall A, Hasdai D, Wallentin L, Battler A, Rosengren A (2005) Diabetes mellitus: clinical presentation and outcome in men and women with acute coronary syndromes. Data from the Euro Heart Survey ACS. *Diabetic Medicine* **22**(11): 1542–50

DIABETES CARE



ACE inhibitors and ARBs prevent new-onset type 2 diabetes

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

1 Given that angiotensin II increases hepatic glucose production and decreases insulin sensitivity, it is plausible that angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) may reduce new-onset type 2 diabetes.

2 A systematic literature search was conducted for results (between 1966 and September 2004) from randomised controlled trials of ACE inhibitors or ARBs with new-onset type 2 diabetes as an end point.

3 Based on 11 trials (and 66608 trial participants), these antihypertensives were found to prevent new-onset type 2 diabetes (odds ratio [OR], 0.78; 95% confidence interval [CI], 0.73–0.83).

4 Considered individually, the ORs were 0.79 (95% CI, 0.71–0.89) for ACE inhibitors, based on six trials, and 0.76 (95% CI, 0.70–0.82) for ARBs, based on five trials.

5 No significant reductions were found in mortality, cardiovascular events or cerebrovascular events among individuals who had hypertension.

Gillespie EL, White CM, Kardas M, Lindberg M, Coleman CI (2005) The impact of ACE inhibitors or angiotensin II type 1 receptor blockers on the development of new-onset type 2 diabetes. *Diabetes Care* **28**(9): 2261–6

'These findings link hyperglycaemia to CV outcomes and thus add to evidence suggesting that glucose lowering may reduce CV risk.'

'The presence of diabetes in women with acute coronary syndromes was associated with a greater likelihood of presenting with ST elevation, developing Q-wave myocardial infarction and dying in hospital.'