Cardiovascular journals

Blockade of the renin–angiotensin–aldosterone system reduces risk of end-stage renal disease

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It has previously been suggested that blockade of the renin–angiotensin–aldosterone system results in delay of progression of diabetic nephropathy. However, more recently, some studies have questioned the blockade of this system in renoprotection.

This meta-analysis by Sarafidis et al (summarised alongside) evaluated the effect of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs) in individuals with diabetic nephropathy.

A literature search was undertaken on the Medline/PubMed and Embase databases, to find trials published up to June 2007 that compared the effects of ACEIs or ARBs with placebo, or with a regimen not including ACEIs or ARBs, or both. The effect of the agents on the incidence of end-stage renal disease (ESRD), doubling of the serum creatinine level or death from any cause were evaluated in diabetic nephropathy. Of 1028 initially identified studies, 24 fulfilled the inclusion criteria (20 using ACEIs and four using ARBs).

The use of ACEIs was associated with a trend towards the reduction of ESRD (relative risk 0.70), and the use of ARBs with a significant reduction of ESRD risk (relative risk 0.78; $P=0.002$). Both drug classes were associated with a reduction in the risk of doubling the serum creatinine level, but neither affected all-cause mortality.

These data support the use of agents blocking the renin–angiotensin–aldosterone system in reducing the rate of progression of renal impairment to ESRD. While it is a shame that neither agent affected all-cause mortality, this finding was not entirely unexpected.

EUROPEAN HEART JOURNAL

Diabetes a risk factor for adverse outcomes in heart failure, regardless of ejection fraction

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

1 This study investigated the difference in risk associated with heart failure in people with diabetes with low versus preserved ejection fraction (EF); a total of 7599 individuals with a broad range of EFs were included in this study and assessed for diabetes, and subsequent heart failure was recorded.

2 A total of 28.3% of those with preserved EF (defined as EF>40%) had diabetes, compared with 28.5% in those with low EF (defined as <40%).

3 People with diabetes and preserved EF were at increased risk of cardiovascular-related death or hospitalisation for heart failure (hazard ratio [HR] 2.0 [1.70-2.36]) compared with those with low EF (HR 1.60 [1.44-1.77]; interaction test $P=0.0009$).

4 Risk of all-cause mortality was similar in all people with diabetes, regardless of EF.

5 Overall, diabetes was deemed to be an independent predictor of cardiovascular morbidity and mortality in individuals with heart failure, regardless of low or preserved EF; the relative risk of cardiovascular-related death or hospitalisation due to heart failure associated with diabetes is significantly increased in those with preserved EF compared with those with low EF.

MacDonald MR, Petrie MC, Varyani F et al (2008) Impact of diabetes on outcomes in patients with low and preserved ejection fraction heart failure: an analysis of the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) programme. *European Heart Journal* **29**: 1377–85

AMERICAN JOURNAL OF HYPERTENSION

Renoprotective effects of RAAS blockers

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

1 This meta-analysis investigated available data on treatment with renin–angiotensin–aldosterone system (RAAS) blockers (angiotensin-converting enzyme inhibitors [ACEIs] and angiotensin-receptor blockers [ARBs]) in diabetes-related nephropathy.

2 The authors used the Medline/Pubmed and Embase databases to conduct a systematic literature search in order to identify controlled trials that compared the effects of ACEIs or ARBs with placebo. They also identified those trials that examined a regimen that did not include a RAAS blocker on the incidence of end-stage renal disease, doubling of serum creatinine level or death from any cause.

3 The literature search identified 1028 possible studies, of which 24 fulfilled the inclusion criteria, giving a total patient population of 10 598 individuals.

4 ACEI treatment was associated with a trend towards a reduced incidence of end-stage renal disease (though it was not statistically significant, $P=0.08$), and treatment with ARBs was associated with a significant decrease in risk of end-stage renal disease ($P=0.002$). Both classes conferred a statistically significant reduction in the risk of doubling the serum creatinine level ($P=0.006$; $P=0.001$, respectively).

5 Overall mortality was not affected by either RAAS blocker, and therefore the authors conclude that ACEIs and ARBs can be used interchangeably for renoprotection in diabetes.

Sarafidis PA, Stafylas PC, Kanaki AI et al (2008) Effects of renin-angiotensin system blockers on renal outcomes and all-cause mortality in patients with diabetic nephropathy: an updated meta-analysis. *American Journal of Hypertension* **21**: 922–9

AMERICAN JOURNAL OF CARDIOLOGY

Diabetes and HHE might increase risk of CAD in women

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

1 Some hypotheses link reproductive hormones with an increased incidence of coronary artery disease (CAD) in women with diabetes. This study aimed to clarify the association between diabetes, hypothalamic hypooestrogenaemia (HHE), and the incidence of CAD.

2 A total of 95 pre-menopausal women underwent coronary angiography for suspected ischaemia, and were evaluated over a median period of 5.9 years.

3 The authors found that presence of diabetes is associated with HHE (P<0.05); the combined presence of diabetes and HHE is indicative of increased incidence of severe CAD (P= 0.008).

Ahmed B, Bairey Merz CN, Johnson BD et al (2008) Diabetes mellitus, hypothalamic hypoestrogenemia, and coronary artery disease in premenopausal women (from the National Heart, Lung, and Blood Institute sponsored WISE study). *American Journal of Cardiology* **102**: 150–4

INTERNATIONAL JOURNAL OF CARDIOLOGY

Fenofibrate cost-effective in long-term CVD prevention

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

1 This study evaluated the economic effect of preventative therapy with fenofibrate in middle-aged patients with diabetes and a higher incidence of cardiovascular disease (CVD).

2 The authors performed an economic analysis from the FIELD (Fenofibrate Intervention and Event Lowering in Diabetes) study pooled data.

3 Compared with placebo, treatment with fenofibrate was found to result in an approximately 10% net saving in overall healthcare costs; based on the observed rates of CVD in the study group, additional treatment with fenofibrate had a financial impact ranging from a24% saving to a 4% net increase.

4 The authors suggest that fenofibrate therapy in middle-aged people, possibly in combination with a statin, confers financial benefit from a reduction in expensive cardiac procedures.

Carrington M, Stewart S (2008) Is fenofibrate a cost-saving treatment for middle-aged individuals with type II diabetes? An economic analysis of the FIELD Study. *International Journal of Cardiology* **127**: 51–6

AMERICAN HEART JOURNAL

Atrial fibrillation increases risk of ischaemic stroke

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

1 This study was undertaken in order to provide an estimate of the prevalence and incidence of chronic atrial fibrillation (CAF) in the UK. The study was also designed to test the accuracy of the Congestive heart failure, Hypertension, Age >75, Diabetes mellitus, and prior Stroke or transient ischemic attack (CHADS2) risk stratification score for predicting stroke.

2 The authors identified a study population of 51 087 individuals with CAF from the GP Research Database.

3 It was found that the incidence of CAF increased over time and by age, and was higher in men than women. Adding sex and age categories improved the CHADS2 score.

4 In conclusion, CAF is a growing problem that increases the risk of stroke. CHADS2 is a useful measure, but could be improved.

Rietbrock S et al (2008) Chronic atrial fibrillation: Incidence, prevalence, and prediction of stroke using the Congestive heart failure, Hypertension, Age >75, Diabetes mellitus, and prior Stroke or transient ischemic attack (CHADS2) risk stratification scheme. *American Heart Journal* **156**: 57–64

EUROPEAN HEART JOURNAL

300mg/day aspirin or clopidogrel for adequate platelet inhibition in people with diabetes

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

1 This study compared the effects of aspirin treatment at 300mg/day with those of combined treatment with aspirin 100mg/day and clopidogrel 75mg/day on the platelet function of people with diabetes and coronary artery disease.

2 A total of 151 individuals with diabetes and coronary artery disease, and an impaired antiplatelet response to aspirin at 100mg/day were included in this study. Participants were randomly allocated to receive either aspirin 300mg/day or aspirin 100mg/day plus clopidogrel 75mg/day, and aggregation tests were repeated after 2 weeks.

3 Inadequate response to aspirin was found in 60 individuals; both those receiving aspirin 300mg/day and those in the combination treatment group had a significant reduction in platelet aggregation.

4 Combination treatment was more effective for the treatment of platelet aggregation than aspirin alone (P=0.002).

5 Increasing aspirin dose or adding clopidogrel to existing aspirin therapy rectified an initially impaired response to aspirin 100mg/day (P<0.001).

6 Addition of clopidogrel to existing aspirin treatment is the most effective treatment method for platelet inhibition (P<0.05).

Duzenli MA, Ozdemir K, Aygul N et al (2008) Comparison of increased aspirin dose versus combined aspirin plus clopidogrel therapy in patients with diabetes mellitus and coronary heart disease and impaired antiplatelet response to low-dose aspirin. *American Journal of Cardiology* **102**: 396–400

> *"Addition of clopidogrel to existing aspirin treatment is the most effective treatment method for platelet inhibition."*

"A significant association was established between diabetes and waist circumference and LV hypertrophy (P=0.01)."

EUROPEAN HEART JOURNAL

Changing risk of heart disease in people with diabetes

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

1 This authors of this study evaluated figures from four national surveys in Finland, in order to assess changes in the rate of coronary heart disease (CHD) and mortality associated with diabetes.

2 Data from the two earliest surveys were combined and compared with the combined data from the two latest surveys, providing a 10-year gap between baseline assessments, and an overall follow-up period of 10 years.

3 Incidence of CHD in women was similar between the two cohorts; incidence of CHD in men with diabetes was decreased in the later patient cohort. However, the relative risk of CHD-related mortality was increased in men with diabetes.

Barengo NC, Katoh S, Moltchanov V et al (2008) The diabetes-cardiovascular risk paradox: results from a Finnish population-based prospective study. *European Heart Journal* **29**: 1889–95

AMERICAN JOURNAL OF CARDIOLOGY

Percutaneous coronary intervention and risk of nephropathy

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

1 This study aimed to assess the incidence and outcome of nephropathy after percutaneous coronary intervention (PCI) in people with diabetes.

2 A total of 570 individuals with diabetes and normal serum creatinine levels who underwent PCI between August 2004 and December 2006 were included in this study.

3 After 6 months, 12.3% of participants developed post-PCI nephropathy, most of whom were female.

4 Those individuals with post-PCI nephropathy also had a significantly increased incidence of major adverse cardiac events ($P<0.001$).

Roy P, Raya V, Okabe T et al (2008) Incidence, predictors, and outcomes of post-percutaneous coronary intervention nephropathy in patients with diabetes mellitus and normal baseline serum creatinine levels. *American Journal of Cardiology* **101**: 1544–9

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Leptin only independent marker of coronary artery calcification

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

1 This study investigated whether or not plasma levels of leptin and adiponectin are indicative of coronary artery calcification (CAC). The authors also investigated which markers of insulin resistance and adiposity best predicted CAC.

2 A total of 860 individuals without diabetes were included in this study.

3 Plasma adiponectin and leptin were associated with adiposity, insulin resistance and inflammation. However, after adjustment for age, gender and traditional risk factors, only leptin was found to be associated with an increased incidence of CAC in the study population.

4 Overall, leptin and the homeostasis model assessment of insulin resistance index were the strongest markers of CAC.

Qasim A, Mehta NN, Tadesse MG et al (2008) Adipokines, insulin resistance, and coronary artery calcification. *Journal of the American College of Cardiology* **52**: 231–6

AMERICAN JOURNAL OF CARDIOLOGY

Type 2 diabetes is associated with left ventricular hypertrophy

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

1 Whether or not type 2 diabetes is associated with left ventricular (LV) hypertrophy, defined as an increase in LV mass that is independent of body size, is not known. The authors of this study investigated the incidence of LV hypertrophy in a multiethnic cohort, in order to identify an independent association with diabetes.

2 A total of 1932 people, both with and without diabetes (n=443 and n=1489, respectively) were included in this study; LV mass was calculated in all participants by transthoracic echocardiography.

3 Using a multivariable analysis to associate the incidence of diabetes with LV hypertrophy, results were adjusted for confounding factors such as age, gender, race, BMI, history of coronary heart disease and alcohol consumption.

4 LV mass, BMI and systolic blood pressure were higher in people with diabetes ($P<0.001$), and type 2 diabetes was independently associated with increased LV mass ($P=0.03$).

5 Risk of LV hypertrophy was significantly increased in individuals with type 2 diabetes ($P=0.004$), but no association was determined between BMI and the incidence of LV hypertrophy. However, a significant association was established between waist circumference and LV hypertrophy in people with type 2 diabetes ($P=0.01$).

Eguchi K, Boden-Albala B, Jin Z et al (2008) Association between diabetes mellitus and left ventricular hypertrophy in a multiethnic population. *American Journal of Cardiology* **101**: 1787–91