Major journals

Albuminuria and cardiovascular risk

Miles Fisher, Consultant Physician, Glasgow Royal Infirmary

Large multicentre studies are difficult to organise and expensive to run. It is now common for these trials to spawn multiple publications, and recent angiotensin converting enzyme (ACE) inhibitor and angiotensin receptor blocker studies are no exception.

The LIFE (Losartan Intervention For End-point reduction) study compared cardiovascular outcomes in a large group of hypertensive patients with left ventricular hypertrophy treated with either losartan or atenolol. Over 9000 patients were studied, and more than 1000 patients with diabetes were included. The composite outcome comprised myocardial infarction, stroke and cardiovascular death. Losartan was more effective than atenolol in reducing the composite endpoint in the study as a whole, and in the patients with diabetes who were studied as a separate subgroup.

The LIFE group study examines the baseline urine albumin-creatinine ratio (UACR) as a predictor of subsequent cardiovascular events. Around 90% of patients had baseline urinary albumin samples for inclusion in the present analysis. To stratify risk, patients were divided into deciles of urinary albumin, with the lowest decile a ratio <0.25, and the top three deciles 2.53–4.31, 4.32–9.92, and >9.43. For every 10-fold increase in the UACR in patients without diabetes the hazard ratio for the composite endpoint increased by 57%. There was no specific threshold for increased risk. Risk increased at much lower levels than previously reported in patients with diabetes. The median UACR was higher in patients with diabetes at 3.05 vs. 1.16 mg/mmol in patients without diabetes. Again for every 10-fold increase in UACR there was an increase in the hazard ratio for the composite endpoint, but this was slightly less at 39%.

The UACR can now join blood pressure, cholesterol, blood glucose and HbA_{1c} as a continuous variable that predicts cardiovascular outcomes even within the so-called normal range.

ANNALS OF INTERNAL MEDICINE

Increased UACR results in increased cardiovascular risk

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

1 Albuminuria is associated with increased risk for fatal and non-fatal cardiovascular events, independent of conventional risk factors.

2 The objective of this prospective study was to determine whether the relation between albuminuria and cardiovascular risk can be used to predict cardiovascular morbidity and mortality in patients with hypertension.

3 Renal glomerular permeability was evaluated in 8206 patients with hypertension and left ventricular hypertrophy using the urine albumin–creatinine ratio (UACR). Patients were randomly assigned to double-blind therapy with losartan or atenolol in this multicentre cohort study.

4 As UACR increased, risk for subsequent cardiovascular events in patients with hypertension continuously increased, and there appears to be no unique thresholds at which increased albuminuria predicts cardiovascular morbidity and mortality.

5 Cardiovascular risk increases at much lower UACR values in these patients than has been reported among patients with diabetes.

6 Detecting microalbuminuria might help the clinician decide when to initiate antihypertensive therapy because identification of target organ damage is an indication for treatment in patients with lower blood pressure.

Wachtell K, Ibsen H, Olsen MH et al (2003) Albuminuria and cardiovascular risk in hypertensive patients with left ventricular hypertrophy: the LIFE study. *Annals of Internal Medicine* 139: 901–06

ANNALS OF INTERNAL MEDICINE

High plasma homocysteine levels predict CHD risk

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

1 The authors investigated whether moderately elevated plasma homocysteine levels are independently related to increased incidence of fatal and non-fatal CHD events in people with type 2 diabetes.

2 The final study sample consisted of 830 Finnish patients with type 2 diabetes, 45–64 years (462 men and 368 women).

3 CHD mortality and incidence of non-fatal myocardial infarction (MI) were recorded during the 7-year follow-up.

4 Participants with plasma homocysteine levels of ≥15 mmol/l at baseline had a higher risk for CHD death that those with plasma homocysteine levels <15 mmol/l. The risks for all CHD events were 36.2% and 22.6%, respectively.

5 In Cox regression analyses, elevated plasma homocysteine level was significantly associated with CHD mortality and all CHD events even after adjustment for confounding variables, including creatinine clearance.

6 In patients without MI at baseline, moderate hyperhomocysteinemia was also associated with CHD mortality and all CHD events in univariate and multivariate Cox regression analyses.

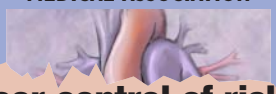
7 In this large cohort of patients with type 2 diabetes, plasma homocysteine level was a strong and independent risk factor for CHD events.

Soinio M, Marniemi J, Laakso M, Lehto S, Rönnemaa T (2004) Elevated plasma homocysteine level is an independent predictor of coronary heart disease events in patients with type 2 diabetes mellitus. *Annals of Internal Medicine* 140: 94–100

'HbA_{1c} levels, blood pressure and total cholesterol levels were compared between patients from these surveys to assess whether control of risk factors for vascular disease has changed.'

'In total, only 7.3% of adults with diabetes in NHANES 1999–2000 attained recommended goals. Further public health efforts are needed to control risk factors for vascular disease among people diagnosed with diabetes.'

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION



Poor control of risk factors for vascular disease in diabetes

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

1 The objectives were to examine US data from the Third National Health and Nutrition Examination Survey (NHANES III) conducted from 1988–94, and the NHANES 1999–2000 on control of risk factors for vascular disease among adults (≥20 years) with previously diagnosed diabetes.

2 Patients included those that had participated in both the interview and examination in either NHANES III (n=1265) or NHANES 1999–2000 (n=441). HbA_{1c} levels, blood pressure and total cholesterol levels were compared between patients from these surveys to assess whether control of risk factors for vascular disease has changed.

3 In NHANES 1999–2000, only 37.0% of patients achieved the target goal of HbA_{1c} level <7.0%, and 37.2% were above the 'take action' HbA_{1c} level of >8.0%; these percentages did not change significantly from NHANES III.

4 In NHANES 1999–2000, only 35.8% of participants achieved the target of systolic blood pressure <130 mmHg and diastolic blood pressure <80 mmHg, and 40.4% had hypertensive blood pressure levels; these percentages did not change significantly from NHANES III.

5 Over half (51.8%) of the participants in NHANES 1999–2000 still had total cholesterol levels of ≥200 mg/dL.

6 In total, only 7.3% of adults with diabetes in NHANES 1999–2000 attained recommended goals. Further public health efforts are needed to control risk factors for vascular disease among people diagnosed with diabetes.

Saydah SH, Fradkin J, Cowie CC (2004) Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. *Journal of the American Medical Association* 291: 335–42

BRITISH MEDICAL JOURNAL

Low insulin resistance linked with depression

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

1 This study assessed the association between insulin resistance and depression in 4286 women aged 60–79 years.

2 Insulin resistance is a determinant of free fatty acids in the blood, which are in turn important in tryptophan metabolism and brain serotonin concentrations. Individuals who are insulin resistant may have higher serotonin concentrations and be less likely to be depressed.

3 It was found that the prevalence of depression decreased linearly with increasing insulin resistance among women without diabetes, and then increased among women with diabetes.

4 There may be an indication for assessing depressive symptoms among patients receiving treatments that affect insulin resistance.

Lawlor DA, Davey Smith G, Ebrahim S (2003) Association of insulin resistance with depression: cross-sectional findings from the British women's heart and health study. *British Medical Journal* 327: 1383–4

AMERICAN JOURNAL OF MEDICINE

Calcium antagonists safe for hypertension with diabetes

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

1 From a MEDLINE database search, 14 studies were identified that reported the effects of calcium antagonists in hypertensive patients with diabetes.

2 The effect of treatment with calcium antagonists on morbidity and mortality in comparison with placebo, conventional therapy and therapy that blocks the renin-angiotensin system were estimated from these studies.

3 Compared with placebo, calcium antagonists reduced cardiovascular morbidity and mortality.

4 Calcium antagonists are safe and effective in reducing most types of cardiovascular morbidity and mortality in hypertensive patients with diabetes, although their use is associated with a lesser reduction of risk of heart failure than other treatments for hypertension.

Grossman E, Messerli FH (2004) Are calcium antagonists beneficial in diabetic patients with hypertension? *American Journal of Medicine* 116: 44–9

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

High CACS predicts CHD risk compared with FRS alone

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

1 This study determined whether coronary artery calcium score (CACS) combined with Framingham risk score (FRS) among asymptomatic adults provides prognostic information superior to either method alone.

2 Of 1461 asymptomatic participants (>45 years) with at least one abnormal coronary risk factor, 1312 underwent computed tomography (CT) examination for measurement of CACS. Of these, 269 had diabetes, 12 had coronary events before the CT scan and 2 had missing data; thus, 1029 people were studied.

3 There were 291 patients with a FRS >20%, and 221 with a CACS >300. Compared with a FRS <10%, a FRS >20% predicted the risk of MI or CHD death; compared with a CACS of 0, a CACS >300 was predictive. The CACS significantly modified the risk prediction in all categories of a FRS ≥10%, but not when the FRS was <10%.

4 Data support the hypothesis that a high CACS can modify predicted risk obtained from FRS alone.

Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC (2004) Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. *Journal of the American Medical Association* 291: 210–15