

Cardiovascular journals

Diabetes lessens the response of LVH to treatment



Mark Kearney, Cardiologist, Department of Cardiovascular Research, University of Leeds, Leeds

The presence of left ventricular hypertrophy (LVH) measured using voltage criteria on the 12-lead electrocardiogram (ECG) or echocardiograph is an independent risk factor for cardiovascular mortality (including sudden death) and morbidity (including myocardial infarction and chronic heart failure). This risk applies across a range of patients.

Studies have shown that people with type 2 diabetes mellitus who also have hypertension have more severe LVH than people with hypertension but normal glucose tolerance.

With the prevalence of type 2 diabetes and the metabolic syndrome approaching epidemic proportions, an important and unanswered question is: how does the presence of type 2 diabetes affect the response of LVH to antihypertensive treatments?

The Losartan Intervention For Endpoint (LIFE) Reduction in Hypertension Study explored the effect of losartan compared with atenolol on mortality and morbidity in hypertensive patients with LVH. The present report (see right)

examined the effect of these treatments on regression of LVH in people with and without diabetes.

Diabetes was present in over 1000 of 9193 people. People with diabetes were older, more obese and more likely to have comorbidities. After a follow-up of about 5 years, during which time blood pressure and ECG LVH was assessed at 6-monthly intervals, people with diabetes had less regression of LVH and had significantly higher rates of cardiovascular mortality, myocardial infarction, stroke and all-cause mortality. The regression of LVH was associated with a 17–35% reduction in event rate in people without diabetes. This improved outcome in response to LVH regression was not demonstrated in those with diabetes.

These results may explain at least in part the poorer outcome in hypertensive people with diabetes. The results probably also illustrate that a multifactorial approach to the management of people with a high risk of diabetes is necessary, focusing on a range of factors (including inflammation, glycaemia and lipids), with LVH being just one of them. The present report, while very interesting, as usual in type 2 diabetes, raises more questions than it answers.

CIRCULATION



Lesser regression of ECG LVH in diabetes

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

1 The presence and severity of left ventricular hypertrophy (LVH) detected by 12-lead electrocardiography (ECG) strongly predicts cardiovascular (CV) morbidity and mortality.

2 Hypertensive people with diabetes have a higher prevalence and greater severity of LVH than those without diabetes.

3 However, it is unclear whether diabetes itself attenuates regression of hypertensive LVH, and whether regression of ECG LVH, defined with Cornell Product (CP) criteria, has similar prognostic value in people with and without diabetes.

4 Diabetes was present in 1195 people out of a total of 9193 hypertensive participants in the Losartan Intervention For Endpoint (LIFE) Reduction in Hypertension Study.

5 People were treated with losartan or atenolol and followed up with serial ECG and blood pressure determinations at baseline, 6 months and yearly until death or study end.

6 After a mean follow-up of 4.8 years, people with diabetes had less regression of CP LVH, remained more likely to have LVH by CP criteria and had higher rates of CV death, myocardial infarction, stroke and all-cause mortality than those without diabetes.

7 The absence of a demonstrable improvement in prognosis in people with diabetes in response to regression of ECG LVH suggests a more complex interrelation between underlying LV structural and functional abnormalities and outcome in these people.

Okin PM, Devereux RB, Gerds E et al (2006) Impact of diabetes mellitus on regression of electrocardiographic left ventricular hypertrophy and the prediction of outcome during antihypertensive therapy. *Circulation* **113**: 1588–96

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Met S in the elderly increases CV risk

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

1 The study assessed whether the metabolic syndrome (Met S) predicted a higher risk of cardiovascular (CV) events in 3035 participants in the Health, Aging and Body Composition Study, aged 70–79 years.

2 Over 6 years there were 434 deaths, 472 coronary events, 213 myocardial infarctions (MI) and 231 heart failure (HF)

hospital stays, with 59% having at least one hospital stay.

3 People with the Met S were at a significantly higher risk of coronary events (19.9% versus 12.9%), MI (9.1% versus 5.7%), HF (10.0% vs 6.1%) and overall hospital stays (63.1% versus 56.1%) than those without (all $P < 0.001$).

4 There were no significant differences in overall mortality between the groups, although there was a trend toward higher CV mortality (5.1% versus 3.8%) and coronary mortality (4.5% versus 3.2%) in people with the Met S.

5 People over 70 years are at a high risk of CV events; Met S in this group is associated with a greater risk.

Butler J, Rodondi N, Zhu Y et al (2006) Metabolic syndrome and the risk of cardiovascular disease in older adults. *Journal of the American College of Cardiology* **47**: 1595–602

CIRCULATION

CHD risk factors predict fatality

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

- This study used data gathered systematically and prospectively before coronary heart disease (CHD) events to examine acute CHD mortality among 5888 adults in the Cardiovascular Health Study.
- During a median follow-up of 8.2 years, 985 CHD events occurred, of which 30% were fatal.
- There was no difference in case fatality by race and gender, but it was higher with age (≥ 80 years) and prior CHD.
- Case fatality decreased slightly over time (ranging from 28–30% per year in the early 1990s to 23% by 2000–2001). With adjustment for age at myocardial infarction (MI) and gender, there was a 6% lower odds of fatality with each successive year, and a 25% lower odds of fatality with each successive 4-year period.
- People with fatal events were older, were more likely to have a history of CHD, MI, congestive heart failure (CHF), diabetes and hypertension, and had more evident sub-clinical disease by most measures compared with those with non-fatal events.
- Prior CHF, regardless of left ventricular systolic function, age, gender or prior CHD, conferred a ≥ 3 -fold increased risk of fatality in almost all subgroups.
- In older people, CHD case fatality remains substantial, with easily identifiable risk factors that may be different from those that predict incident disease.

Pearte CA, Furberg CD, O'Meara ES et al (2006) Characteristics and baseline clinical predictors of future versus non-fatal coronary heart disease events in older adults. *Circulation* **113**: 2177–85

EUROPEAN HEART JOURNAL

Glucose level linked with endothelial function

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

- Vascular endothelium is a major organ involved in hyperglycaemia and is affected by asymmetric dimethylarginine (ADMA), which is an endogenous, competitive inhibitor of nitric oxide synthase.
- The concentration of ADMA is increased by tumour necrosis factor- α (TNF- α), which is an important factor in the pathogenesis of type 2 diabetes.
- This study investigated whether intensive therapy for hyperglycaemia might improve endothelial function in association with the modulation of the cytokines or decrease in plasma ADMA level in 24 people with type 2 diabetes.
- No significant glycaemia or flow-mediated, endothelium-dependent dilation (FMD) changes were noted in 10 people on conventional diabetes treatment.
- In the 14 people who received intensive treatment for hyperglycaemia and who had a significantly decreased glucose level, FMD increased significantly, with a significant decrease in TNF- α and ADMA levels.
- Intensive treatment of hyperglycaemia is associated with the improvement of endothelial function, coupled with a decrease in plasma TNF- α and ADMA levels in people with type 2 diabetes.

Yasuda S, Miyazaki S, Kanda M et al (2006) Intensive treatment of risk factors in patients with type 2 diabetes mellitus is associated with improvement of endothelial function coupled with a reduction in the levels of plasma asymmetric dimethylarginine and endogenous inhibitor of nitric oxide synthase. *European Heart Journal* **27**: 1159–65

EUROPEAN HEART JOURNAL

CAC imaging predicts CV events

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

- This study determined the prevalence and clinical predictors of subclinical atherosclerosis and myocardial ischaemia in uncomplicated type 2 diabetes, and assessed their relationship to short-term outcome.
- Established risk factors and coronary artery calcium (CAC) scores were prospectively measured in 510 asymptomatic people with type 2 diabetes without prior cardiovascular (CV) disease.
- Of those people with type 2 diabetes, 46.3% had evidence of coronary calcification (CAC scores >10 Agatston units [AU]), a reliable marker of coronary atherosclerosis.
- All people with a CAC score >100 AU ($n=127$) and a random sample of 53 people with a CAC score ≤ 100 AU underwent myocardial perfusion scintigraphy (MPS).
- Twenty events occurred during a median follow-up of 2.2 years. No CV events occurred in people with a CAC score <10 AU, with most events occurring in those with severe CAC (>400 AU).
- The age, systolic blood pressure, duration of diabetes, UK Prospective Diabetes Study risk score, CAC score and extent of myocardial perfusion abnormality were significant predictors of time to CV events in a univariable Cox proportional hazard model.
- Conventional CV risk factors have limited value for predicting silent myocardial ischaemia. CAC and MPS are superior methods for the prediction of short-term CV events.

Anand DV, Lim E, Hopkins D et al (2006) Risk stratification in uncomplicated type 2 diabetes: prospective evaluation of the combined use of coronary artery calcium imaging and selective myocardial perfusion scintigraphy. *European Heart Journal* **27**: 713–21

‘Of those people with type 2 diabetes, 46.3% had evidence of coronary calcification, a reliable marker of atherosclerosis.’

‘Intensive treatment of hyperglycaemia is associated with the improvement of endothelial function, coupled with a decrease in plasma tumour necrosis factor alpha and asymmetric dimethylarginine levels in people with type 2 diabetes.’

‘Multivariate analysis showed that diabetes, male gender and a history of any prior procedure remained strong predictors of increased per cent atheroma volume.’

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Some CV risk factors predict atherosclerosis

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

1 The relationship between established cardiovascular (CV) risk factors and the extent of atherosclerosis was investigated.

2 Clinical characteristics, quantitative coronary angiography and intravascular ultrasound (IVUS) were evaluated in 654 people.

3 Plaque areas were measured at 1 mm intervals to determine atheroma volume, and data on CV risk factors were collected.

4 Atheroma volume averaged 174.5mm³, and the per cent atheroma volume averaged 38.9%.

5 For the entire group, 81.2% of all cross-sections were atherosclerotic.

6 Univariate analysis showed a strong association between male gender, non-Caucasian race and history of prior revascularisation with atherosclerotic burden.

7 A history of diabetes or hypertension, prior myocardial infarction and age were also predictors of more severe disease; LDL-cholesterol and C-reactive protein were not predictors of disease severity.

8 Multivariate analysis showed that diabetes, male gender and a history of any prior procedure remained strong predictors of increased percent atheroma volume; prior stroke, non-Caucasian race and smoking remained significant.

9 Compared with IVUS, there was a more limited relationship between risk factors and angiographic measures of disease severity.

Nicholls SJ, Tuzcu EM, Crowe T et al (2006) Relationship between cardiovascular risk factors and atherosclerotic disease burden measured by intravascular ultrasound. *Journal of the American College of Cardiology* **47**: 1967–75

‘Metabolic syndrome strongly predicts cardiac morbidity and mortality in healthy people with a family history of coronary artery disease.’

CIRCULATION

Magnesium lowers risk of Met S

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

1 The authors prospectively examined the relation between magnesium (Mg) intake and incidence of the metabolic syndrome (Met S) in 4637 adults aged 18–30 years who were free from the Met S and diabetes at baseline.

2 A total of 608 incident Met S cases were identified during the 15 years of follow-up.

3 After adjustment for potential confounders, Mg intake was found to be inversely associated with the risk of incident Met S.

4 People in the two highest quartiles of Mg intake had a significantly lower risk of Met S.

5 Young adults with an increased Mg intake have a lower risk of developing the Met S.

He K, Liu K, Daviglus ML et al (2006) Magnesium intake and incidence of metabolic syndrome among young adults. *Circulation* **113**: 1675–82

CIRCULATION

Increased PAI-1 linked with diabetes

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

1 A total of 1224 people with (n=381) and without diabetes (n=843) from the Insulin Resistance Atherosclerosis Study were studied to determine the relation of incident diabetes to dynamic changes in plasminogen activator inhibitor-1 (PAI-1) and fibrinogen (FIB) levels.

2 After 5.2 years, diabetes developed in 140/843 people (16.6%).

3 Baseline and follow-up levels of PAI-1 and FIB were higher in people with diabetes versus those without diabetes.

4 Progression of PAI-1 levels over time in healthy people without diabetes was associated with incident diabetes after adjusting for demography, smoking and baseline PAI-1 levels.

5 In contrast, change in FIB was not significantly related to incident diabetes.

6 These findings add to the current knowledge on the relation of fibrinolysis and coagulation abnormalities to the development of type 2 diabetes.

Festa A, Williams K, Tracy RP et al (2006) Progression of plasminogen activator inhibitor-1 and fibrinogen levels in relation to incident type 2 diabetes. *Circulation* **113**: 1753–9

AMERICAN JOURNAL OF CARDIOLOGY

Metabolic syndrome predicts CV risk

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

1 The authors investigated whether the metabolic syndrome (Met S) augments the risk for major cardiovascular (CV) events in 1316 healthy people with a family history for coronary artery disease (CAD).

2 During 2 years, the incidence of first CV events was compared between those with and without the Met S at baseline.

3 Specifically, in people aged ≤50 years, having the Met S conferred a 5.8-fold increased relative risk for first CV events.

4 Obesity was strongly associated with incident myocardial infarction.

5 MS strongly predicts cardiac morbidity and mortality in healthy people with a family history of CAD.

Reinhard W, Holmer SR, Fischer M et al (2006) Association of the metabolic syndrome with early coronary disease in families with frequent myocardial infarction. *American Journal of Cardiology* **97**: 964–7