

Cardiovascular journals

Diabetes may reduce the female cardioprotective effect



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The global prevalence of type 2 diabetes is set to double over the next 30 years, with cardiovascular disease accounting for more than 75% of type 2 diabetes-related mortality. Indeed, it was suggested that the risk of death from coronary heart disease (CHD) among people with diabetes but no prior myocardial infarction (MI) is similar to that among people without diabetes but with prior MI. This observation, however, has been challenged by subsequent studies. Thus far, no study has compared the impact of diabetes and MI at baseline and during follow-up on CHD mortality with adjustment for major cardiovascular disease (CVD) risk factors.

The aim of Hu *et al* (see right) was to investigate the independent and joint effects of diabetes and MI at baseline and during follow-up on CHD, CVD, non-CVD and total mortality. To assess these issues, two studies were conducted: a baseline cohort study including prior diabetes or MI; and a follow-up cohort study including patients with incident diabetes or MI during follow-up. Men with a history of MI at baseline were at higher risk of CHD and total mortality than men with a history of diabetes at baseline, while women with prior MI at baseline were at lower risk of CHD and total mortality than those with prior diabetes. When the disease status during

follow-up was considered, men and women with incident MI had higher CHD mortality but similar risk of all-cause mortality in comparison with people with incident diabetes.

The magnitude of the effects of diabetes and MI on CHD risk is likely to depend on the duration of disease and this time factor may operate differently for diabetes than MI, since many CHD risk factors are present prior to the onset of type 2 diabetes. Among patients who survived an MI, the highest risk occurs right after the event, whereas in people with diabetes the risk increases over time, reflecting the natural history of the condition and the effect of exposure to various CHD risk factors characteristic of type 2 diabetes (such as hyperglycaemia, insulin resistance and the typical atherogenic dyslipidaemia).

The observations of this study support the hypothesis that the presence of diabetes reduces the usual cardioprotective effect of being female with respect to CHD, which may in part be accounted for by the relatively greater detrimental effect of obesity on vascular risk in women. More aggressive treatment may thus be particularly needed in women with diabetes; and women with diabetes may particularly benefit from intensive risk factor modification.

The results of this study may have important clinical implications. For instance, treatment strategies should be considered based on individual disease status, particularly type 2 diabetes for women and future CVD risk.

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY



Mortality effects of diabetes and MI are sex specific

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

- Sex-specific data on the relative effects of diabetes and myocardial infarction (MI) on coronary heart disease (CHD) and all-cause mortality are scarce.
- A baseline cohort study was conducted in 2416 people with prior diabetes or MI, and a follow-up cohort study was carried out in 4315 people with incident diabetes or MI (diagnosed during follow-up).
- For men in the baseline cohort, mortality risk was higher with MI than diabetes for both CHD (hazard ratio [HR], 1.78; 95% confidence interval [CI], 1.39–2.27) and all causes (HR, 1.22; 95% CI, 1.03–1.44).
- For women in the baseline cohort, mortality risk was lower with MI than diabetes for both CHD (HR, 0.57; 95% CI, 0.39–0.82) and all causes (HR, 0.55; 95% CI, 0.43–0.70).

- For men in the follow-up cohort, mortality risk was higher with MI than diabetes for CHD (HR, 2.15; 95% CI, 1.70–2.73) but similar for all causes (HR, 0.95; 95% CI, 0.82–1.11).
- Likewise, for women in the follow-up cohort, mortality risk was higher with MI than diabetes for CHD (HR, 1.65; 95% CI, 1.27–2.14) but similar for all causes (HR, 1.02; 95% CI, 0.84–1.23).
- These results have important implications for clinical practice, state the authors.

Hu G, Jousilahti P, Qiao Q, Peltonen M, Katoh S, Tuomilehto J (2005) The gender-specific impact of diabetes and myocardial infarction at baseline and during follow-up on mortality from all causes and coronary heart disease. *Journal of the American College of Cardiology* 45(9): 1413–8

INTERNATIONAL JOURNAL OF CARDIOLOGY

Diabetes increases mortality in people with ACS without ST elevation

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

- It has been shown that for people with ST elevation myocardial infarction, having diabetes worsens the prognosis.

- This prospective, multicentre study (n=1046) examined people with acute coronary syndromes (ACS) without ST elevation.
- In the participants, diabetes was linked to significant mortality: over 6 months, one in eight will die; and over 4 years, one in three will die.
- The authors use these and other results to support more aggressive management of these high-risk patients.

Bakhai A, Collinson J, Flather MD, de Arenaza DP, Shibata MC, Wang D *et al* (2005) Diabetic patients with acute coronary syndromes in the UK: high risk and under treated. Results from the prospective registry of acute ischaemic syndromes in the UK (PRAIS-UK). *International Journal of Cardiology* 100(1): 79–84

STROKE



Trunk-to-peripheral fat ratio predicts stroke

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

1 The relationship that excess weight and its distribution around the body has with the risk of stroke needs clarification.

2 A large, prospective cohort study was carried out to examine this in middle-aged men (n=9151) followed up for stroke mortality over 23 years.

3 The measures of excess weight and its distribution used were body mass index (BMI), subscapular skinfold thickness (SSF) and the ratio of subscapular to triceps skinfold thickness (SFR; serving as a trunk-to-peripheral fat ratio).

4 When controlling for just age, BMI, SSF and SFR were all significantly associated with stroke mortality risk; respectively, the hazard ratios (HRs) were 1.17 (95 % confidence interval [CI], 1.06–1.30), 1.12 (95 % CI, 1.01–1.25) and 1.14 (95 % CI, 1.03–1.26).

5 After additional adjustments for systolic blood pressure, diabetes, smoking and socioeconomic status, however, only SFR's association remained significant (HR, 1.11; 95 % CI, 1.01–1.23).

6 Finally, after further adjustment for BMI, this association was still significant (HR, 1.11; 95 % CI, 1.00–1.23).

6 Thus, an indicator of the relative distribution of peripheral and trunk fat has been shown to be linked to stroke mortality, even after controlling for other risk factors.

Tanne D, Medalie JH, Goldbourt U (2005) Body fat distribution and long-term risk of stroke mortality. *Stroke* **36**(5): 1021–5

HEART



Opportunities to reduce CVD risk in diabetes have been missed

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

1 It is several years since guidelines on cardiovascular disease (CVD) risk identified people with type 2 diabetes (or type 1 diabetes with microalbuminuria) as a priority group for preventative therapy for CVD.

2 Two prospective cohort studies were conducted to determine if opportunities to address CHD risk had been taken in people with diabetes.

3 From 1998 to 2001, 4286 women and 4252 men aged between 60 and 79 were studied.

4 The risk of CHD was considered to have been addressed if the participants had received aspirin, statins, β -blockers, angiotensin-converting enzyme (ACE) inhibitors or blood pressure (BP)-lowering drugs.

5 In primary prevention, for both men and women, all of the interventions had been given to a significantly greater proportion of people with diabetes than people without.

6 In secondary prevention, though, most interventions had not been given to a significantly greater proportion of people with diabetes.

7 The exceptions were BP-lowering drugs in women (odds ratio [OR], 2.05; 95 % confidence interval [CI], 1.07–3.93) and ACE inhibitors in both women (OR, 2.32; 95 % CI, 1.23–4.37) and men (OR, 2.14; 95 % CI, 1.32–3.47).

Emberson JR, Whincup PH, Lawlor DA, Montaner D, Ebrahim S (2005) Coronary heart disease prevention in clinical practice: are patients with diabetes special? Evidence from two studies of older men and women. *Heart* **91**(4): 451–5

AMERICAN JOURNAL OF HYPERTENSION



Vasodilating β -blockers do not increase diabetes risk in heart failure

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

1 The resistance to insulin's metabolic activity that is associated with sympathetic nervous system (SNS) overactivity accompanies heart failure caused by left-ventricular systolic dysfunction.

2 Some of the treatments for chronic heart failure that work by blocking the SNS have been linked to the development of new-onset diabetes.

3 β -blockers, for instance, have a varying effect on glucose and lipid metabolism depending on individual agents' receptor specificity.

4 This report investigated β -blockers using a MEDLINE literature search of articles through May 2004.

5 First-generation β -blockers (non-selective β_1 - and β_2 -blockers such as timolol and propranolol) have been linked to an increased risk of the development of diabetes over 10 years.

6 The second-generation β -blockers metoprolol and atenolol (β_1 -selective blockers) have been shown to reduce insulin sensitivity and total body glucose uptake during a euglycaemic hyperinsulinaemic clamp test.

7 Third-generation β -blockers (carvedilol, celiprolol and dilevalol), which are vasodilators, are associated with general improvements in insulin sensitivity and decreased atherogenic changes of serum lipids.

Kostis JB, Sanders M (2005) The association of heart failure with insulin resistance and the development of type 2 diabetes. *American Journal of Hypertension* **18**(5 Pt 1): 731–7

CIRCULATION

Pioglitazone reduces carotid IMT independently of glycaemic control

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

1 Two pilot studies have linked pioglitazone to reduced levels of the cardiovascular risk marker carotid intima-media thickness (IMT) in people with type 2 diabetes.

2 This study further investigated this effect of pioglitazone-based therapy (45 mg/day), comparing it with glimepiride-based therapy (2.7 ± 1.6 mg/day) in 173 people.

3 After 12 weeks, carotid IMT had a greater reduction with pioglitazone (-0.033 ± 0.052 mm) than with glimepiride (-0.002 ± 0.047 mm; $P < 0.01$ between groups).

4 This result was independent of improved glycaemic control.

Langenfeld MR, Forst T, Hohberg C, Kann P, Lubben G, Konrad T et al (2005) Pioglitazone decreases carotid intima-media thickness independently of glycaemic control in patients with type 2 diabetes mellitus: results from a controlled randomized study. *Circulation* **111**(19): 2525–31

INTERNATIONAL JOURNAL OF CARDIOLOGY

Stroke risk factors identified in elderly

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

1 With ischaemic/non-embolic strokes accounting for over 80% of all strokes in older people, identifying major risk factors is an important objective.

2 This study looked at 163 consecutive patients (older than 70 years) admitted to hospital with a first

ischaemic/non-embolic stroke as well as 166 healthy controls.

3 Among the factors identified by multivariate logistic regression analysis as significantly associated with a first ischaemic/non-embolic stroke were diabetes (odds ratio [OR], 1.92; 95% confidence interval [CI], 1.02–3.63) and the metabolic syndrome (OR, 2.48; 95% CI, 1.16–5.29).

4 These and other associations identified by the study could be addressed with lifestyle modifications and therapeutic intervention.

Milionis HJ, Liberopoulos E, Goudevenos J, Bairaktari ET, Seferiadis K, Elisaf MS (2005) Risk factors for first-ever acute ischemic non-embolic stroke in elderly individuals. *International Journal of Cardiology* **99**(2): 69–75

CIRCULATION

Atorvastatin and irbesartan may remedy endothelial dysfunction

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

1 Post-meal hyperglycaemia and hypertriglyceridaemia are known risk factors for cardiovascular disease, with their effect believed to be due to endothelial dysfunction.

2 It is also known that statins and angiotensin I receptor blockers can improve endothelial function, reducing oxidative stress and inflammation.

3 The results of this study (which was carried out in 20 people with type 2 diabetes and 20 controls) confirmed the effect of hypertriglyceridaemia and hyperglycaemia on endothelial function.

4 Moreover, atorvastatin and irbesartan were found to alleviate the effect, especially in combination.

Ceriello A, Assaloni R, Da Ros R, Maier A, Piconi L, Quagliaro L et al (2005) Effect of atorvastatin and irbesartan, alone and in combination, on postprandial endothelial dysfunction, oxidative stress, and inflammation in type 2 diabetic patients. *Circulation* **111**(19): 2518–24

‘Third-generation β -blockers [...], which are vasodilators, are associated with general improvements in insulin sensitivity and decreased atherogenic changes of serum lipids.’

‘Among the factors identified by multivariate logistic regression analysis as significantly associated with a first ischaemic/non-embolic stroke were diabetes [...], and the metabolic syndrome.’