

Cardiovascular disease

Gemfibrozil offers an alternative to statin therapy



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The role of statins in the reduction of cardiovascular disease in people with diabetes is well established from post-hoc subgroup analysis of several large studies. However, the typical dyslipidaemia of diabetes comprising raised triglycerides, a low HDL cholesterol, and relatively normal LDL cholesterol, should be more responsive to treatment with fibrates. This study by Rubins and colleagues describes a post-hoc subgroup analysis from the Veterans Affairs High-Density Lipoprotein Intervention Trial (VA-HIT), where 2531 patients with established coronary heart disease received either gemfibrozil or placebo.

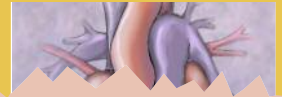
The entry criteria comprised low levels of HDL cholesterol and total cholesterol. Twenty-five per cent of the participants had known diabetes, a further 6% had undiagnosed diabetes, based on a fasting plasma glucose concentration ≥ 7 mmol/l, and 13% had impaired fasting glucose. The risk of the composite endpoint was highest

in those with diagnosed diabetes, which in turn was only slightly greater than for those with undiagnosed diabetes. All groups benefited from treatment with gemfibrozil, and the absolute reduction in participants with diabetes was greater, although this did not reach statistical significance.

In an additional part of the study, 1733 participants without diabetes were categorised into quartiles based on their fasting plasma insulin levels at the start of the study. Event rates were higher in the highest quartile of fasting plasma insulin. Again, the benefit from gemfibrozil appeared to be greater in this group.

For patients with diabetes and insulin resistance with the typical diabetic dyslipidaemia, gemfibrozil offers an alternative to statin therapy. Comparative studies are required to determine whether fibrates or statins offer the best overall treatment, and whether the combined use of these agents offers increased benefit when major cardiovascular endpoints are examined.

ARCHIVES OF INTERNAL MEDICINE



Gemfibrozil lowers risk of major cardiovascular events

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

- This study set out to examine glucose and insulin status and the risk of major cardiovascular outcomes, and to determine the efficacy of gemfibrozil in subjects with varying levels of glucose tolerance or insulin resistance.
- Subgroup analyses were carried out on data from the Department of Veterans Affairs High-Density Lipoprotein Intervention Trial (VA-HIT).
- This randomised controlled trial included 2531 men with coronary heart disease (CHD), a high-density lipoprotein cholesterol level of 40 mg/dl or less and a low-density lipoprotein cholesterol level of 140 mg/dl or less.

- Subjects were given 1200 mg/day gemfibrozil or placebo and were followed up for composite end-point (CHD death, stroke or myocardial infarction) for an average of 5.1 years.
- Risk was greater in subjects with known and newly diagnosed diabetes than in subjects with a normal fasting glucose level.
- Gemfibrozil reduced the risk of composite end-point in subjects with diabetes by 32%. The reduction in CHD death was 41%.
- In subjects without diabetes gemfibrozil was most effective in reducing the risk of composite end-point in those with the highest fasting plasma insulin level quartile (risk reduction = 35%).

Rubins HB, Robins SJ, Collins D et al (2002) Diabetes, plasma insulin, and cardiovascular disease. *Archives of Internal Medicine* **162**: 2597-604

JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY



Diabetes is risk factor for early death after surgery

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

- Diabetes has not previously been investigated as a risk factor for early and late cardiac-related death after coronary bypass surgery in multivessel disease.
- This study considered 767 patients with diabetes and 2593 without diabetes who were operated on between January 1988 and December 1999.

- Early (30-day) mortality and long-term (5-year) freedom from death were assessed.
- Early mortality was 2.2%, while early cardiac mortality was 1.3%. Diabetes was an independent risk factor for early cardiac death.
- Five-year survival was 93.5%, while five-year freedom from cardiac death was 96.3%. Diabetes was an independent risk factor.

- But if only the subjects who survived the first 30 days after surgery are considered, long-term survival is not statistically different for patients with and without diabetes, and diabetes is no longer a risk factor. Diabetes is only a risk factor for early death following surgery.

Calafiore AM, Di Mauro M, Di Giammarco G et al (2003) Effect of diabetes on early and late survival after isolated first coronary bypass surgery in multivessel disease. *Journal of Thoracic and Cardiovascular Surgery* **125**: 144-54

‘There was a progressive increase in potassium levels in all patients with increasing duration of chest pain... this was attenuated in diabetic patients’

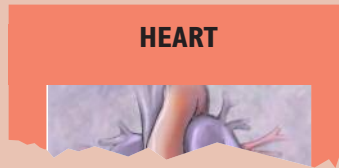


Rosiglitazone reduces urinary albumin excretion

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

- 1 Microalbuminuria in patients with type 2 diabetes is an early indicator of renal and cardiovascular disease.
- 2 This study compared the effect of rosiglitazone and glyburide on urinary albumin excretion (UAE) in 203 patients with type 2 diabetes in a 52-week open-label cardiac safety study.
- 3 Urinary albumin:creatinine ratio (ACR) was measured at baseline and after 28 and 52 weeks' treatment.
- 4 ACR was significantly reduced in both groups after 28 weeks, but only in the rosiglitazone group after 52 weeks.
- 5 Rosiglitazone was thus associated with a decrease in UAE.

Bakris G, Viberti G, Weston WM et al (2003) Rosiglitazone reduces urinary albumin excretion in type II diabetes. *Journal of Human Hypertension* 17: 7–12

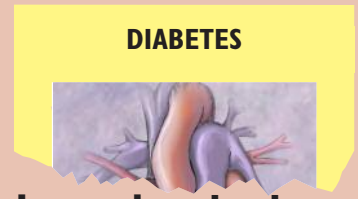


Higher serum potassium levels in diabetic patients

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

- 1 Hypokalaemia is common in patients presenting with acute coronary syndromes.
- 2 This prospective cohort study compared serum potassium levels in 2428 patients presenting with acute coronary syndromes.
- 3 The mean serum potassium concentration was significantly higher in patients with diabetes.
- 4 There was a progressive increase in potassium levels in all patients with increasing duration of chest pain; this was attenuated in patients with diabetes and those who had been pretreated with beta-blockers.
- 5 Increased potassium serum in patients with diabetes may be due to sympathetic nerve dysfunction.

Foo K, Sekhri N, Deaner A et al (2003) Effect of diabetes on serum potassium concentrations in acute coronary syndromes. *Heart* 89: 31–5



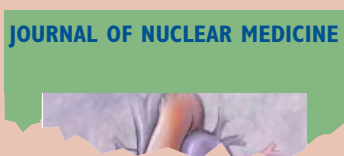
Lower heart rate variability linked to CHD in diabetes

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

- 1 A reduced heart rate variability (HRV) has been shown to be associated with a higher risk of cardiovascular disorders.
- 2 The aim of this study was to test for a link between low HRV and a risk of developing coronary heart disease (CHD) and also non-CHD mortality, and to determine whether this relationship is greater in people with diabetes.
- 3 A prospective cohort study was carried out with 11 654 men and women aged 45–64 years from the Atherosclerosis Risk in Communities Study.
- 4 Supine resting 2-min HRV data were measured at baseline examination.
- 5 There were 635 cases of CHD including 346 cases of myocardial infarction (MI) and 82 cases of fatal CHD, and 623 deaths unrelated to CHD over 8 years of follow-up.
- 6 Among those with diabetes, hazards ratios were 2.03, 1.60, 1.50 and 1.27 for MI, CHD, fatal CHD and non-CHD deaths, respectively, comparing the lowest quartile to the top three quartiles of high frequency.
- 7 No similar association was found for those without diabetes.
- 8 A lower HRV was found to be related to the development of CHD among those with diabetes, independent of the duration or severity of glucose metabolism impairment.

Liao D, Carnethon M, Evans GW et al (2002) Lower heart rate variability is associated with the development of coronary heart disease in individuals with diabetes. *Diabetes* 51: 3524–31

‘A lower heart rate variability was found to be related to the development of CHD among those with diabetes.’



Assessing endothelial dysfunction with dipyridamole

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

- 1 This study compared cold pressor testing (CPT) and dipyridamole on coronary blood flow (CBF) measured by PET in 10 patients with type 2 diabetes and 10 control subjects. Angiotension-converting enzyme (ACE) inhibition was also examined.

- 2 Resting CBF was similar in both groups. CPT increased CBF in controls but not in type 2 diabetes patients.
- 3 Dipyridamole increased CBF in both groups, although the increase was higher in controls.
- 4 ACE inhibitor had no effect. Adding CPT caused a small increase in CBF in patients with type 2 diabetes. Adding dipyridamole led to the same increase in CBF in both groups.
- 5 Dipyridamole may be more useful than CPT for measuring endothelial dysfunction.

Kjaer A, Meyer C, Nielsen FS et al (2003) Dipyridamole, cold pressor test, and demonstration of endothelial dysfunction: a PET study of myocardial perfusion in diabetes. *Journal of Nuclear Medicine* 44: 19–23