

Gemfibrozil reduced the risk for coronary events in men with coronary artery disease and low levels of high-density lipoprotein cholesterol

Rubins HB, Rubins SJ, Collins D, et al., for the Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. *N Engl J Med.* 1999 Aug 5;341:410-8.

QUESTION

Is gemfibrozil effective for secondary prevention of coronary artery disease (CAD) events in men with low levels of both high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol?

DESIGN

Randomized {allocation concealed*}, †blinded (patients, outcome assessors, and study personnel),* placebo-controlled trial with median follow-up of 5.1 years (Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial [VA-HIT]).

SETTING

20 Veterans Affairs medical centers in the United States.

PATIENTS

2531 men who were < 74 years of age (mean age 64 y); had a documented history of CAD; had no serious comorbid conditions; and had an HDL cholesterol level \leq 40 mg/dL (1.0 mmol/L), an LDL cholesterol level \leq 140 mg/dL (3.6 mmol/L), and a triglyceride level \leq 300 mg/dL (3.4 mmol/L).

INTERVENTION

1264 men were allocated to gemfibrozil, 1200 mg/d, and 1267 were allocated to placebo.

MAIN OUTCOME MEASURES

The main outcome was combined incidence of nonfatal myocardial infarction (MI) or death from CAD. Secondary outcomes included stroke and all-cause mortality.

MAIN RESULTS

Analysis was by intention to treat. Patients in the gemfibrozil group had a lower risk for the combined end point of nonfatal MI or CAD death and for investigator-designated stroke (Table) than did patients in the placebo group; groups did not differ for all-cause mortality (15.7% vs 17.4%, $P = 0.23$).

CONCLUSION

Among men with coronary artery disease and low levels of both high-density and low-density lipoprotein cholesterol, gemfibrozil reduced the risk for the combined end point of nonfatal myocardial infarction or death from coronary artery disease.

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*See Glossary.

†Information provided by author.

Gemfibrozil vs placebo for secondary prevention of coronary artery disease (CAD) in men with low levels of high-density lipoprotein cholesterol†

Outcomes at 5 y	Gemfibrozil	Placebo	RRR (95% CI)	NNT (CI)
Nonfatal myocardial infarction or CAD death	17.3%	21.7%	22% (7 to 35)	23 (13 to 74)
Stroke	5.1%	6.9%	29% (2 to 48)	56 (27 to 725)

‡Abbreviations defined in Glossary; NNT and CI provided by author.

COMMENTARY

The results of the VA-HIT should change practice. Clinicians should no longer be complacent when patients with coronary disease have low HDL cholesterol levels (\leq 40 mg/dL) as well as LDL cholesterol levels below guideline-recommended thresholds for treatment. Women with lipid profiles similar to the men in this study should also benefit from treatment. The failure to show a reduction in all-cause mortality is not an important weakness; the sample size was not calculated to show this reduction. A larger study would probably show this reduction, as have other studies of cholesterol-lowering therapies.

An alternative strategy for this patient population is the use of statins to lower LDL cholesterol levels to 70 to 80 mg/dL. In a small study of 341 patients, Pitt and colleagues (1) found that patients who had LDL cholesterol levels reduced to a mean of 77 mg/dL from about 145 mg/dL with atorvastatin had fewer ischemic events than patients treated with angioplasty and standard lipid management. The Scandinavian Simvastatin Survival Study showed a treatment benefit in patients with baseline LDL cholesterol levels of approximately 140 mg/dL; notably, HDL cholesterol levels increased 8% with simvastatin (2). Whether similar benefits

from statins would be found in patients with LDL cholesterol levels of approximately 110 mg/dL—the mean level in VA-HIT patients—is unknown.

When treating patients with CAD who have normal LDL and low HDL cholesterol levels, evidence for using gemfibrozil is now stronger than for using statins. If a statin is used, clinicians should check for an increase in HDL cholesterol level of \geq 6%, as seen in the VA-HIT. An alternative to medication might be weight loss and exercise if an equivalent 6% increase in HDL cholesterol levels can be achieved.

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References

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2. Pedersen TR, Olsson AG, Faergeman O, et al. Lipoprotein changes and reduction in the incidence of major coronary heart disease events in the Scandinavian Simvastatin Survival Study (4S). *Circulation.* 1998;97:1453-60.