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THE FUTURE FOR CARDIOVASCULAR DISEASE IN DIABETES AND THE METABOLIC SYNDROME

While overall cardiovascular mortality decreased during the late 1990s, mortality in those with diabetes does not appear to have changed dramatically. This raises the question as to whether this reflects inadequacy of therapies used or the insufficient application of these treatments to patients with diabetes. Alternatively, does it reflect too narrow an approach to therapies and definition of these patients?

Currently, our treatments focus on glycaemic control, reducing hypertension and lowering lipids in patients with established type 2 diabetes. Perhaps it is time to extend consideration of increased cardiovascular risk to a wider spectrum of patients with the metabolic syndrome, and evaluate patients with diabetes as a sub-group of those with the metabolic syndrome. Given the cluster of risk factors in the metabolic syndrome, and the potential for these patients to progress to type 2 diabetes, will the current prevalence and epidemic of the metabolic syndrome limit the success of strategies aimed at reducing cardiovascular disease?

In cohorts of patients with cardiovascular disease, those with the metabolic syndrome represent a large proportion. The presence of the metabolic syndrome increases the rate of complication after a cardiovascular event.

For example, in a cohort of patients with symptoms of coronary artery disease, the metabolic syndrome was found to be present in 51 % of them, and the severity of coronary disease increased with the number of features of the syndrome (Solymoss et al, 2004). In an unselected population of patients with acute myocardial infarction, approximately 46 % of the patients fulfilled the criteria for the metabolic syndrome. The risk of development of subsequent heart failure increases with features of the metabolic syndrome and, indeed, hyperglycaemia (Zeller et al, 2005). In a further analysis of the 4S study, event rates in the placebo group were greater in those patients with the metabolic syndrome than those without the metabolic syndrome. However, a greater reduction in the adverse outcomes with simvastatin was noted in those with the metabolic syndrome.

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In the Helsinki Heart and VA-HIT studies, reductions in cardiovascular events were considerably greater for those individuals with a body mass index (BMI) >26 kg/m^2 compared with those with a BMI <26 kg/m^2, indicating that the presence of insulin resistance appears to increase the benefit of fibrate therapy. In those with a BMI >26 kg/m^2, there was a continual increase in the protective effect of gemfibrozil with not only increasing BMI, but also increasing waist circumference and fasting insulin levels.

The soon to be presented PROACTIVE study may of course provide initial data on the specific efficacy of peroxisome proliferator-activated receptor (PPAR)-α/-γ agonism and insulin sensitisation on cardiovascular event prevention in a high-risk group of patients with type 2 diabetes. Other newer agents will allow for more targeted therapy, such as with novel PPAR agonists or cannabinoid-1 receptor blockade. The latter, with rimonabant, certainly appears to result in clinically significant weight loss, and improvement in waist circumference, lipid levels and insulin resistance.

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