

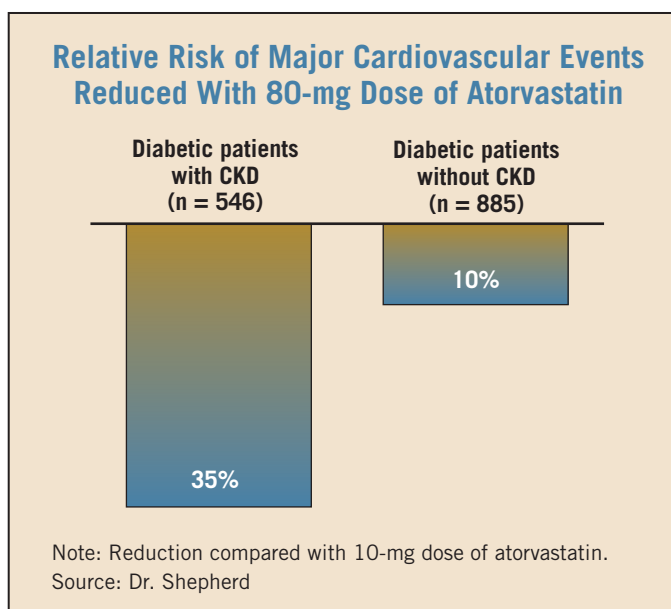
# Diabetics With CKD Benefit From Atorvastatin

BY MIRIAM E. TUCKER  
Senior Writer

CHICAGO — Intensive lipid lowering with high-dose atorvastatin significantly reduced the incidence of major cardiovascular events in coronary patients who have both type 2 diabetes and chronic kidney disease, Dr. James Shepherd reported at the annual scientific sessions of the American Diabetes Association.

In a new subanalysis of diabetic patients in the Pfizer-funded Treating to New Targets (TNT) study, “Individuals got greater benefit in relative terms and far greater benefit in absolute terms if they had the combination of diabetes and renal disease, because they had much greater risk to begin with,” said Dr. Shepherd, professor and head of pathological biochemistry at the Royal Infirmary and the University of Glasgow (Scotland).

The main finding of the TNT study of 10,001 patients with stable coronary heart disease was a 22% reduction in the risk of major cardiovascular events with the use of 80 mg of atorvastatin per day relative to 10 mg/day at a median follow-up of 5 years (*N. Engl. J. Med.* 2005;352:1425-35). A subsequent subanalysis of the 1,501 diabetic patients in that study showed a 25% event reduction with 80 mg versus 10 mg (*Diabetes Care* 2006;29:1220-6). However, another study of 1,255 patients who had type 2 diabetes and end-stage renal disease (ESRD) and were undergoing hemodialysis showed no cardiovascular benefit of 20 mg of atorvastatin per day, compared with placebo (*N. Engl. J. Med.* 2005;353:238-48).



To further investigate the potential role of atorvastatin treatment in patients with both diabetes and kidney disease, Dr. Shepherd and his associates analyzed the TNT outcomes of 1,431 of the diabetic patients in the study for whom renal data were available. There were 546 patients with chronic kidney disease (CKD)—defined as having an estimated glomerular filtration (eGFR) rate of less than 60 mL/min per 1.73 m<sup>2</sup>—and 885 with normal kidney function (eGFR of at least 60 mL/min per 1.73 m<sup>2</sup>).

At baseline, those with CKD had greater cardiovascular morbidity than those without, including higher sys-

tolic blood pressure (136.1 vs. 133.6 mm Hg); a greater proportion had a history of hypertension (76% vs. 67%), as well as higher rates of peripheral vascular disease, coronary bypass grafting, and congestive heart failure. There were also more women in the CKD group (42% vs. 18%). The 80-mg dose of atorvastatin lowered LDL cholesterol equally in both groups, from about 98 mg/dL at baseline to 75 mg/dL at follow-up, Dr. Shepherd reported.

Major cardiovascular events (coronary heart disease death, nonfatal myocardial infarction, resuscitation after cardiac arrest, fatal or nonfatal stroke) occurred in 13.4% of the diabetics with normal GFR and 17.4% of those with both diabetes and CKD. (The rates were 7.8% among those without diabetes or CKD and 10% for the nondiabetics with CKD.) Compared with 10 mg of atorvastatin, the 80-mg dose reduced the relative risk of major cardiovascular events by 35% in the diabetic patients with CKD, compared with just 10% among the diabetics without CKD. “Those with the greatest risk got the greatest benefit from intensive intervention with atorvastatin,” Dr. Shepherd commented.

The drug was well tolerated overall, with no evidence of myopathy. “The high dose of atorvastatin created no penalty with regard to side effects,” he noted.

When asked by an audience member why atorvastatin did not benefit the patients with ESRD in the earlier study, Dr. Shepherd responded, “I think it’s a function of the degree of kidney compromise. If you have patients with ESRD on dialysis, you’re asking far too much of a drug to reverse that. But you can see a reversal if you have compromise but still-viable glomerular filtration rates.” ■

## Supplemental Olive Oil May Cut Cardiac Risk in Diabetes

BY HANNAH BROWN  
Contributing Writer

BARCELONA — Additional supplementation of olive oil in the diets of patients with type 2 diabetes may reduce their risk of cardiac problems, according to research presented at an international congress on prediabetes and metabolic syndrome.

In a preliminary study to identify a potential mechanism through which the Mediterranean diet protects against cardiovascular disease, Dr. Mohammed Hammami, head of the biochemistry laboratory, faculty of medicine, Monastir, Tunisia, and colleagues analyzed the relationship between homocysteine and other modifiable cardiovascular risk factors, including diet, in type 2 diabetes patients.

Previous work has linked high levels of homocysteine to a high prevalence of macroangiopathy, coronary heart disease, and renal insufficiency in patients with type 2 diabetes. In addition, clinical trials testing vitamin supplementation in these patients have resulted in decreased homocysteine levels in patients with diabetic dyslipidemia, suggesting that lowering homocysteine levels could reverse the lipid problems.

The researchers recruited 70 patients with type 2 diabetes and evaluated their nutritional habits based on a validated food frequency questionnaire. On average, those with diabetes consumed foods high in fat. Dr. Hammami and his col-

leagues measured mean homocysteine levels, which were 13.6 plus or minus 6.06 micromol/L for the group; 27.5% of participants had levels of plasma homocysteine assessed as high (greater than 15 micromol/L). Further studies showed an inverse correlation between homocysteine levels and dietary saturated fatty acids or daily cholesterol intake.

According to Dr. Hammami, plasma homocysteine levels were lower in patients with diabetes who consumed extra virgin olive oil than in those who consumed little or none (10 micromol/L vs. 14 micromol/L, respectively). “Our study supports other studies showing the beneficial effects of the Mediterranean diet on the cardiovascular risk factors, essentially on homocysteine levels,” he said.

“We have revealed a potential mechanism by which a Mediterranean type of diet may affect coronary risk,” Dr. Hammami continued. “The consumption of olive oil, the major fat in this diet type, may lead to decreased levels of homocysteine.”

He suggested that his study “should be followed up by investigations on the effects of the different components of olive oil”—not only oleic acid but also minor components such as vitamins and polyphenols—“on the reduction of homocysteine levels.” Dr. Hammami said he plans to do more extensive patient recruitment and supplementary analysis on such things as thiolactonase activity measurement. ■

## Waist Circumference Predicts Risk of Cardiovascular Events

BY HANNAH BROWN  
Contributing Writer

BARCELONA — Although body mass index is a poor predictor of mortality from myocardial infarction in patients with diabetes, this measure should not be discounted altogether, Dr. Jonathan Shaw said at an international congress on prediabetes and metabolic syndrome.

“Within every tertile of BMI there is increasing risk with increasing waist-to-hip ratio, and with every tertile of waist-to-hip ratio there is increasing risk with [increasing] BMI, so both parameters give different information,” said Dr. Shaw, who is director of clinical research at Australia’s Monash University, Clayton, Victoria. However, he added, BMI, waist-to-hip ratio, and waist circumference “are just proxy measures for the real problem: visceral obesity.”

Analyses of epidemiologic data looking at how BMI and waist-hip ratio predict cardiac dysfunction, such as those presented in the Heart Outcomes Prevention Evaluation study (*N. Engl. J. Med.* 2000;342:145-53), suggest that although BMI has little relation to mortality, there is a stronger association for waist circumference and waist-to-hip ratio. “Two individuals with the same BMI and waist circumference can have different depositions of visceral fat, so measurements of central obesity might be better at predicting MI than BMI,” Dr. Shaw said.

So how good is waist circumference at predicting risk? According to Dr. Shaw,

Japanese data from 2002 (*Circ. J.* 2002;66:987-92) show a correlation between waist circumference and visceral fat, although the volume of this fat can vary between 40 cm<sup>3</sup> and 200 cm<sup>3</sup> for the same waist measurement. New data from the Australian Diabetes, Obesity, and Lifestyle (AusDiab) study—a population-based longitudinal study—suggest that waist circumference may precede other changes that increase risk of cardiovascular events.

“Waist circumference was a significant predictor of changes in each of the other parameters, whereas none of the others predicted changes. Therefore, waist circumference seems to come before [the other parameters] and might be close to the core [driver of risk],” Dr. Shaw said.

In addition, cross-sectional associations between waist circumference and other risk factors or components of metabolic syndrome show that with increasing waist circumference, there is increasing prevalence of other risk factors. Dr. Shaw added that although there is little doubt that central obesity predicts cardiovascular disease risk, whether or not waist circumference and waist-to-hip ratio are independent of other risk factors is not yet confirmed.

Data from the AusDiab study reported by Dr. Shaw show that the greatest increases in waist circumference are occurring in younger people, and changes are 50% greater in women than in men. “If there is a target for public health campaigns to modify behavior, it is young women who need to be targeted,” Dr. Shaw said. ■