

IT'S ALL GREEK TO ME

Currently, treatment and management of hyperlipidemia patients is highly variable in different health settings and cultures. Adding structured and aggressive management strategies for patients showed tremendous value in a trial done in Greece.

Study design

The Greek Atorvastatin and Coronary heart disease Evaluation (GREACE) study was a randomized prospective and open-labelled trial, with the intention to study secondary prevention methods in patients with established vascular disease. In the study, 1,600 consecutive patients were randomized to one of two strategies:

- 1) A structured care setting, where patients were randomized to atorvastatin, aiming for low-density lipoprotein cholesterol (LDL-C) < 2.6 mmol/L. Patients were prescribed to atorvastatin, 10 mg daily, and then, every six weeks, titrated up (to a maximum of 80 mg daily); or
- 2) The control arm, which was randomized to "usual care" (*i.e.*, lifestyle changes, including a low-fat diet and exercise, plus any drug treatment deemed necessary by the physician).

The primary end point, a composite of death, non-fatal myocardial infarction (MI), unstable angina (UA), congestive heart failure (CHF), and revascularization (coronary morbidity), was reduced by 50%. The end point occurred in 96 patients (12%) in the structured care group, versus 196 patients (24.5%) in the usual care group, $p < 0.001$. Total mortality occurred in 2.9% of patients in structured care, versus 5.0% of patients in usual care. This translates to a 43% reduction in total mortality, $p=0.0021$. Stroke was cut nearly in half, from 2.1% in the usual care, to 1.1% in the structured care program.

The baseline cholesterol was 6.65 mmol/L, LDL was 4.65 mmol/L, high-density lipoprotein (HDL) was 1.0 mmol/L, and triglycerides (TG) were 2.05 mmol/L. The mean age was 59, with a body mass index (BMI) of 24. Of the patients in the study, 20% had diabetes, and over 80% had a previous MI. All patients were recruited following an acute ischemic syndrome, and started participating, on average, 90 days after their event.

Inclusion criteria and baseline results:

Patients with established cardiovascular disease below the age of 75 were included, provided their LDL-C > 2.6 mmol/L after six weeks of a lipid-lowering diet, and TG level < 4.5 mmol/L.

Exclusion criteria:

The following individuals were excluded: those who did not understand the protocol or who were unwilling to participate, patients with abnormal liver or renal function tests, and individuals with a history of prior hyperlipidemic drug use.

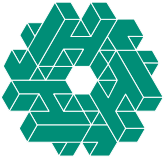
Results

In the structured group randomized to atorvastatin, 95% of patients reached the target LDL-C < 2.6 mmol/L;

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98% of these individuals were on atorvastatin treatment during the entire three years.

To achieve target lipid levels, the mean dose of atorvastatin was 24 mg daily. The breakdown of daily atorvastatin dosage was as follows: 4% of patients were prescribed 10 mg, 80% to 20 mg, 11% to 40 mg, and 3% to 80 mg.

The results were spectacular. Atorvastatin reduced total cholesterol by 36%, LDL-C by 46%, TG by 31%, and non-HDL cholesterol (non-HDL-C) by 44%, while it increased HDL-C by 7%. All these changes were significant.

In the usual care group, 3% of patients reached target LDL-C, and only 14% were on cholesterol-lowering treatment during the entire study, which lasted three years.

All subgroups of patients (women, diabetics, hypertensives, and individuals aged 60 to 75 years, with CHF, recent UA, or prior revascularization) benefited from treatment with atorvastatin in the structured program. Patient withdrawal due to side-effects was low in the structured care group (0.75%), and similar to that of the usual care group (0.4%). Over the three years, one out of every 44 patients avoided cardiovascular death.


How can patient care be improved?

- Make quality control a priority
- Build a multi-factorial system that will work for you
- Obtain baseline data and compare results to guidelines
- Review progress regularly; change strategies as necessary
- Go beyond the status quo: explore new and old tools
- To change behaviour, knowledge is only the starting point
- Develop better patient tools and shared responsibilities
- Continue data collection and practise continuous quality improvement (CQI)
- Ask your patients for feedback

Physician's perspective

The GREACE study is open-labelled and, therefore, has a number of limitations. It is impressive that 95% of the selected patients with established vascular disease could achieve target lipid levels with atorvastatin provided in a structured program. The patients had established heart disease that met both inclusion and exclusion criteria. However, clinical trials tend to select more compliant individuals; I believe that results in one's practice would be less impressive. It is common that patients complain of side-effects and want to stop therapy, even on placebo. For instance, in the Heart Protection Study (HPS), the largest cholesterol trial, 5% of patients on either placebo or active statin therapy complained of sore muscles.

Physicians and patients can do a better job in managing cholesterol disorders by structuring and paying attention to lipid management in high-risk patients (such as those with established vascular disease, and those using higher doses and more potent lipid-lowering agents). By following suggested guidelines, the GREACE study demonstrated a 50% reduction in cardiovascular events, including total mortality.

Keeping healthy is no easy task. It is a shared responsibility between patients and their health-care providers. Patients need to play a more active role in their health management. They should ask their physicians about the best strategies for health maintenance. 

Suggested Reading

1. Athyros VG, Papageorgiou AA, Mercouris BR, et al: Treatment with atorvastatin to the National Cholesterol Educational Program goal versus 'usual' care in secondary coronary heart disease prevention. The Greek Atorvastatin and Coronary heart disease Evaluation (GREACE). *Curr Med Res Opin* 2002; 18(4):220-8.