

Management Strategies of Dyslipidemia in the Elderly: 2005

Source: <http://sci.tech-archive.net/Archive/sci.med.cardiology/2005-10/msg00771.html>

- *From:* "Bill" <xxx@xxxxx>
 - *Date:* Wed, 19 Oct 2005 00:24:35 GMT
-

NOTE: To view the article with Web enhancements, go to:
<http://www.medscape.com/viewarticle/512746>

Management Strategies of Dyslipidemia in the Elderly: 2005

Tarek Helmy, MD; Amar D. Patel, MD; Fadi Alameddine, MD; Nanette K. Wenger, MD, FACC, FAHA

Medscape General Medicine. 2005;7(4):8. ©2005 Medscape
Posted 10/10/2005

Abstract and Introduction

Abstract

During the past 3 years, the treatment of dyslipidemia has evolved significantly. The impact of recent trial data on management strategies in older patients is especially important, because the elderly segment of the US population continues to grow. Several clinical trials have been completed since the publication of the National Cholesterol Education Program (NCEP) Adult Treatment Panel III guidelines were published in 2001. Recent trial data strongly support the use of lipid-lowering therapy in the elderly population. Although therapeutic lifestyle changes remain highly important, supplementation with lipid-lowering therapy has been shown to reduce the risk of cardiovascular events in both primary and secondary prevention models. Compelling data noted from recent clinical trials have prompted the NCEP to publish an updated report that addresses the significant interim developments.

Introduction

Given that several epidemiologic studies have identified the elderly population as having a high risk for cardiovascular events, risk-factor

modification plays an important role in an attempt to reduce adverse cardiovascular events. Management of dyslipidemia in the elderly is of particular clinical relevance, as the population proportion of the aged is becoming greater over time. Even though dyslipidemia is established as one of the major risk factors for the development of coronary artery disease (CAD) in the elderly, most of these data have been derived from large clinical trials that are mainly comprised of middle-aged patients. However, the association between dyslipidemia and CAD holds true for patients over 65 years of age. Large population-based studies, such as the Established Populations for Epidemiology Studies in the Elderly (EPESE), revealed that an elevated total cholesterol level and low high-density lipoprotein cholesterol (HDL-C) level are associated with increased risk of cardiovascular mortality, especially in men.[1,2] Conversely, lower cholesterol levels (as seen in vegetarians) were associated with a lower incidence of CAD and cardiovascular death in patients between the ages of 75 and 84 when compared with nonvegetarians with higher cholesterol levels.[3]

Despite a growing body of evidence regarding the benefits of aggressive reduction of cholesterol levels, older patients with either documented dyslipidemia or significant risk factors for the development of CAD are often underdiagnosed or undertreated. Data from a study conducted in Canada demonstrated that among hospitalized patients at high risk for cardiovascular events, risk-factor assessment and modification were suboptimal, particularly for women and elderly patients.[4] This may be the result of a paucity of evidence regarding the impact of treatment on delaying the progression of atherosclerotic disease in response to screening-guided therapy, concerns of the increased likelihood of adverse events or drug interactions, or doubts regarding the cost-effectiveness of lipid-lowering drug therapy in the elderly population. The National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III report recommends that all adults with blood total cholesterol values above 200 mg/dL be evaluated and that those with elevated low-density lipoprotein cholesterol (LDL-C) levels be treated.[5] Furthermore, no upper age limit should be defined for lipid-lowering interventions in patients with CAD or at increased risk for CAD.[5] Based on the NCEP guidelines, about one third of elderly men and one half of elderly women have elevated cholesterol levels warranting intervention.[6] ATP III expands the indications for intensive cholesterol-lowering therapy in clinical practice. Elevated triglyceride (TG) levels are also considered to be an independent risk factor for developing CAD. Although this was initially difficult to demonstrate in individual studies (mainly due to multiple variables and confounding risk factors),[7] a recent meta-analysis validated the importance of TG as a cardiovascular risk factor.[8,9] As such, the ATP III guidelines now include TG level reduction as a secondary target after LDL-C reduction has been achieved.

Patient Evaluation

Unfortunately, outcome data regarding lipid lowering in the elderly are relatively limited, and the ATP III recommendations for older patients are generally extrapolated from data derived from younger populations. However, emerging clinical trial data from studies, such as the Heart Protection Study (HPS),[10] Anglo-Scandinavian Cardiac Outcomes Trial – Lipid Lowering Arm

(ASCOT–LLA),[11] and Prospective Study of Pravastatin in the Elderly at Risk (PROSPER),[12] provide valuable insight regarding the treatment of dyslipidemia in the elderly.

The first step in selection of LDL–C lowering therapy is to assess the risk status of the individual. Risk determinants, in addition to LDL–C levels, include the presence of CAD (or coronary heart disease [CHD]), other clinical forms of atherosclerotic disease, cigarette smoking, hypertension, age (men > 45 years, women > 55 years), low levels of HDL–C (< 40 mg/dL), and family history of premature coronary disease (CAD in a first–degree male relative < 55 years or a first–degree female relative < 65 years). Based on these risk factors, ATP III outlines 3 risk categories that define the goals and modalities of LDL–C lowering therapy (Table 1). CHD refers to myocardial infarction (MI), angina, coronary revascularization procedures, or clinically evident myocardial ischemia. CHD risk equivalents include clinical forms of atherosclerotic disease other than CAD (peripheral arterial disease, abdominal aortic aneurysm, and symptomatic carotid artery disease), diabetes mellitus, and multiple risk factors (2 or more) that confer a 10–year risk for CHD > 20%.

The NCEP has published a report that reflects the additional clinical trial data that have been published since 2001.[13] Of significance, a new treatment goal that was addressed, as a result of the data from the HPS and Pravastatin or Atorvastatin and Infection Therapy (PROVE–IT)[14] clinical trials, was the potential importance of reducing the LDL–C level to 70 mg/dL in very high risk patients. Individuals who are considered at very high risk are those with known cardiovascular disease plus (1) multiple major risk factors (especially diabetes mellitus), (2) severely and poorly controlled risk factors (especially continued tobacco use), (3) multiple risk factors for the metabolic syndrome, and (4) patients with acute coronary syndromes. Further data to support lower LDL–C goals are provided by the recently published Treating New Targets (TNT) study.[15] For now, LDL–C reduction to < 70 mg/dL remains a therapeutic option on the basis of clinical trial evidence, whereas a goal LDL–C < 100 mg/dL remains their strong recommendation.

Treatment

Nonpharmacologic Interventions

Dyslipidemia can be significantly improved by therapeutic lifestyle changes, such as dietary modification, physical activity, and weight reduction. The potential for diet to prevent cardiovascular disease is often underappreciated by patients. Furthermore, changing ingrained dietary habits is not usually an easy task for most patients. Diet favorably alters the lipid/lipoprotein profile and may allow the use of lower doses of lipid–lowering agents, thus reducing the potential for adverse effects. ATP III recommends reduced intake of saturated fatty acids (< 7% of total calories) with the remainder of total fats from polyunsaturated and monounsaturated fatty acids (25% to 35% of total calories), and intake of less than 200 mg cholesterol/day. The addition of plant stanols/sterols (2 g/day) and soluble fiber (10–15 g/day) can further reduce LDL–C by approximately 10%. Carbohydrates should be limited to 60% of the total daily caloric intake. The Lyon Diet Heart Study is a secondary prevention trial that randomized 605

patients to a Mediterranean-type or a Western-type diet.[16] Despite a similar coronary risk profile between the groups, there was an approximate 50% to 70% relative risk reduction of cardiovascular events (death, MI, stroke, angina, congestive heart failure, and hospitalization) in favor of the Mediterranean-type diet group over a mean follow-up duration of 46 months.

The benefits of the Mediterranean diet were also shown in a prospective study of 22,043 subjects with an age range of 20–86 years. An extensive, validated, food frequency questionnaire was completed at baseline, and subjects were followed for a median of 44 months. Calculation of dietary intake included 14 food groups: potatoes, vegetables, legumes, fruits and nuts, dairy products, cereals, meat, fish, eggs, monounsaturated lipids (mainly olive oil), polyunsaturated lipids (vegetable seed oil), saturated lipids and margarines, sugar and sweets, and nonalcoholic beverages. Evaluation of occupational and leisure-time physical activity was also included. Adherence to the Mediterranean diet was associated with reduced mortality, with a strong association with cardiovascular mortality.[17]

The HALE project was another study evaluating the effects of a Mediterranean diet in the elderly. This included 1507 healthy men and 832 women aged 70–90 years in 11 European countries who were followed for 10 years. A Mediterranean diet, moderate alcohol consumption, moderate-to-high physical activity levels, and nonsmoking were associated with lower mortality rates, including CHD, cardiovascular disease, cancer, and other causes of mortality.[18]

A study by Lemaitre and colleagues[19] investigated the effects of plasma phospholipid concentrations of n–3 polyunsaturated fatty acids (docosahexaenoic acid [DHA]), eicosapentaenoic acid (EPA), and alpha–linolenic acid on ischemic heart disease in elderly patients (age > 65). DHA and EPA are commonly found in fatty fish, whereas alpha–linolenic acid is found in vegetable oils. This was a case–control study nested in the prospective trial of cardiovascular risk factors and outcomes (the Cardiovascular Health Study). Subjects were included if they were free of ischemic heart disease and stroke at baseline, and experienced an MI (fatal or nonfatal) during follow-up. Cases were matched to subjects with the same age, sex, clinical site, and follow-up period in a random fashion. Higher dietary intake of DHA, EPA, and possibly alpha–linolenic acid was associated with a decrease in the incidence of nonfatal ischemic events, when the analysis was adjusted for other coronary risk factors.[19]

Physical inactivity is a major risk factor for CAD.[20] Physical exercise and weight reduction are important elements of therapeutic lifestyle changes, and have a favorable impact on the lipid profile, blood pressure levels, and improve insulin sensitivity. Physical exercise has been reported to reduce the risk of developing CAD by as much as 40%, independent of standard risk-factor modifications.[20] Most patients underestimate their dietary intake and overestimate their level of physical activity and exercise. Scheduled, regular exercise promotes the energy expenditure that is necessary to maintain a desirable body weight. This is especially important because the lifestyles of an increasing percentage of the US population are becoming more

sedentary.

Pharmacologic Management

Several agents are available for lipid lowering, such as hydroxyl-methylglutaryl coenzyme A (HMG CoA) reductase inhibitors ("statins"), nicotinic acid, fibrates, bile acid sequestrants, and intestinal absorption inhibitors, such as ezetimibe. These agents have specific and different effects on the lipid profile. Fibrates lower TG by 20% to 50%, lower LDL-C by 5% to 20%, and raise HDL-C by 10% to 20%. Nicotinic acid lowers LDL-C by 5% to 25%, lowers TG by 20% to 50%, and raises HDL-C by 15% to 35%. Bile acid sequestrants lower LDL-C by 15% to 30%, raise HDL-C by 3% to 5%, and have no consistent predictable effect on TG levels, thus warranting caution in patients with mixed lipid abnormalities with hypertriglyceridemia. Statins lower LDL-C by as much as 50% with some agents, raise HDL-C by 5% to 15%, and lower TG by approximately 30%. Statins also may have "pleiotropic effects" that are independent of lipid lowering. They include vasodilator (through nitric oxide release) and anti-inflammatory effects on vascular endothelial cells, as well as antiproliferative and antimigratory effects on vascular smooth muscle cells. Statins also reduce tissue factor release, inhibit thromboxane activity (leading to inhibition of platelet activation), modulate the recruitment of inflammatory cells, and reduce expression of adhesion molecules in the vascular wall.[21]

Statins are the drug of choice for patients with elevated LDL-C levels. Clinical trials have unequivocally demonstrated that treatment of dyslipidemia with statins reduces cardiovascular events both in patients at high risk for CAD (primary prevention)[10,11,22,23] and in patients with documented CAD (secondary prevention)[10,12,14,15, 24-26] (Table 2). Unfortunately, large multicenter, clinical trials, such as West of Scotland Coronary Prevention Study (WOSCOPS),[22] excluded patients over age 65; the Scandinavian Simvastatin Survival Study (4S)[26] excluded patients older than 70; and the Cholesterol and Recurrent Events (CARE)[24] and Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID)[25] trials excluded patients over the age of 75. Although outcomes data are relatively limited in the elderly, some studies included a sizable elderly cohort. In the 4S trial,[26,27] patients 65 years and older derived more benefit from simvastatin than patients < 65 years (Table 3). A significant reduction in all-cause mortality was evident at 18 months, whereas coronary event rates (coronary death, nonfatal MI, resuscitated cardiac arrest, and silent MI) decreased significantly after 6 months of statin therapy. The CARE trial enrolled 4159 patients (1283 patients aged 65-75) with a history of MI and a serum LDL-C \geq 115 mg/dL.[24] After a 5-year mean follow-up, the incidence of major coronary events (fatal MI, ischemic cardiomyopathy, and sudden death) was reduced by 27% in patients aged 60-75 compared with a 20% reduction in patients younger than age 60. The LIPID trial had similar findings showing that for every 1000 patients treated with pravastatin for 6 years, 133 coronary events were prevented in the 65-75 age group.[25]

The HPS, the largest statin therapy trial conducted to date, randomized 20,563 patients aged 40-80 years (10,697 patients \geq 65 years) with coronary disease, other occlusive arterial disease, or diabetes to either 40 mg of

simvastatin or placebo during a scheduled 5-year treatment period.[10] All-cause mortality was significantly reduced in the simvastatin group, mainly driven by an 18% relative risk reduction in the coronary death rate (MI, ischemic cardiomyopathy, and sudden death) (5.7% vs 6.9%; $P = .0005$). There was a trend toward a reduction in other vascular deaths (.9% vs 2.2%; $P = .07$) and an insignificant reduction in nonvascular deaths (5.3% vs 5.6%; $P = .4$). Furthermore, there was a 25% reduction in the incidence of nonfatal MI or coronary death (8.7% vs 1.8%; $P < .0001$), stroke (44.3% vs 5.7%; $P < .0001$), and coronary or noncoronary revascularization (9.1% vs 1.7%; $P < .0001$). The reduction in major vascular events was not significant during the first year, but was highly significant during each subsequent year. The proportional reduction in the event rate was similar and statistically significant when predesigned subgroup analysis was performed by age (under or over 70 years at study entry). There was also a 27% decrease in stroke incidence. The annual excess risk of myopathy with this regimen was about .01%. There were no significant adverse effects on cancer incidence or on hospitalizations for any nonvascular cause. Statin therapy conferred a decrease in total and cardiovascular mortality without an increase in noncardiovascular mortality. This was true even in patients with baseline LDL-C ≥ 100 mg/dL in a post hoc analysis. The safety profile was identical in both groups and no deterioration in cognitive function was noted.

Another landmark study, PROSPER,[12] randomized an elderly cohort of men and women aged 70–82 years with, or at risk of developing, vascular disease (coronary, cerebral, or peripheral) to pravastatin (40 mg per day; $n = 2891$) or placebo ($n = 2913$). Pravastatin lowered LDL-C concentrations by 34% and demonstrated a 15% relative risk reduction in the composite primary end point of coronary death, nonfatal MI, and fatal or nonfatal stroke over a mean follow-up duration of 3.2 years (hazard ratio, .85; 95% confidence interval [CI], .74–.97; $P = .014$). CHD death and nonfatal MI risk were also reduced (hazard ratio, .81; 95% CI, .69–.94; $P = .006$). Stroke risk was unaffected (hazard ratio, 1.03; 95% CI, .81–1.31; $P = .8$), but the hazard ratio for transient ischemic attack was .75 (95% CI, .55–1.00; $P = .051$). The small number of strokes in this study may explain the lack of statistical significance observed. New cancer diagnoses were more frequent with pravastatin than with placebo (hazard ratio, 1.25; 95% CI, 1.04–1.51; $P = .020$). However, incorporation of this finding in a meta-analysis of all pravastatin and all statin trials showed no overall increase in cancer risk. Mortality from coronary disease fell by 24% ($P = .043$) in the pravastatin group. Pravastatin had no significant effect on cognitive function or disability. The study authors of PROSPER concluded that pravastatin similarly reduces the risk of CAD in elderly patients as demonstrated in younger aged populations. In addition, this study supported the well-documented safety profile and tolerability of statin therapy. Statin drugs appear to have similar efficacy and safety in nonelderly and elderly populations and should be strongly considered for use in elderly patients.[28–30] A soon to be completed study in elderly patients is the Study Assessing Goals in the Elderly (SAGE), which is designed to compare the effects of atorvastatin 80 mg with pravastatin 40 mg on myocardial ischemia, as assessed by Holter monitoring.

New targets for LDL-C reduction, now an optional recommendation from the NCEP-ATP III guidelines, are strongly supported by 2 recent studies. In PROVE-IT, 4162 patients with an acute coronary syndrome were randomized to an aggressive strategy of LDL-C reduction, with high-dose atorvastatin vs usual therapy, with a moderate dose of pravastatin.[14] At 2-year follow-up, the combined end point (time from randomization to death/MI/stroke/coronary revascularization/unstable angina requiring hospitalization) was significantly better in the aggressive therapy group (LDL-C 62 mg/dL) compared with the usual therapy group (LDL-C 95 mg/dL). The recently published TNT trial was the first randomized clinical trial to prospectively assess the efficacy and safety of treating patients with stable CAD to LDL-C levels significantly below 100 mg/dL.[15] The TNT trial compared the effects of a lower goal of LDL-C reduction with high-dose (80 mg) atorvastatin to current LDL goal, with low-dose (10 mg) atorvastatin, and included patients as old as 75 years. At the end of a 5-year follow-up period, the mean LDL-C level in the high-dose atorvastatin group was 77 mg/dL compared with 102 mg/dL in the lower dose group. There was a significant (> 20%) reduction in the primary combined end point of death, MI, and stroke in the lower LDL-C group.

In addition to trials focusing on the use of statin therapy, several studies have also been conducted regarding the therapeutic efficacy of fibrate therapy on secondary prevention. The Veterans Affairs High Density Lipoprotein Cholesterol Intervention Trial (VA-HIT) study evaluated the use of gemfibrozil in patients with low levels of HDL-C. In this trial, 2531 male patients with documented CAD were randomized to gemfibrozil or placebo.[31] During a follow-up period of 5 years, there was a 24% relative risk reduction in the combined outcomes of CHD death, nonfatal MI, or stroke. At 1 year, HDL levels were 6% higher and TG levels were 31% lower in the gemfibrozil group. Further analysis of the data revealed that gemfibrozil therapy was cost-effective and efficacious across a wide age range (55-75 years). Another study of post-MI patients that included a large elderly cohort described a 28% reduction in total mortality in patients treated with the lipid-lowering agents clofibrate and nicotinic acid.[32]

A new class of lipid-lowering drugs is the cholesterol absorption inhibitors. The first drug of this class, ezetimibe, was approved by the US Food and Drug Administration (FDA) in November 2002. It interferes with the absorption of dietary and biliary cholesterol at the intestinal brush border without interfering with uptake of TGs.[33,34] It should be considered as an adjunct to therapy in patients in whom LDL-C reduction is suboptimal, despite maximal statin monotherapy. Ezetimibe can achieve as much as an additional 10% to 15% reduction in the LDL-C level. To date, clinical outcomes data are lacking for ezetimibe, but these trials are ongoing. Although ezetimibe has been administered in the elderly,[35] its therapeutic efficacy has not been specifically evaluated in this population subset.

Combination therapy is also now evolving in which agents targeting different, but usually coexistent, disease processes are combined in a single pill. Observational data have shown that coexistent risk factors, such as hypertension and dyslipidemia, have multiplicative effects on the risk for development of cardiovascular events.[36] The marked relative risk reduction

of adverse cardiovascular events in both the hypertension and lipid-lowering arm of the ASCOT trial prompted a premature termination of both arms of this study. Results from this study as well as the aggressive LDL-C lowering trials have led to the emergence of combination preparations, including combined classes of lipid-lowering agents (simvastatin/ezetimibe), and lipid-lowering and antihypertensive agents (atorvastatin/amlodipine).

Conclusions and Future Directions

Reducing LDL-C has been shown to decrease cardiovascular events to 80 years of age, but studies are needed to explore the efficacy of lipid-lowering therapy in individuals older than 80 years. The magnitude of delay in progression of atherosclerotic disease in response to screening-guided therapy has not been well delineated. The cost-effectiveness of lipid screening in the elderly population, as well as the subgroups that would benefit most from such screening, need to be further studied. Based on ongoing clinical trial data, the guidelines may be modified to recommend that an LDL-C \leq 70 mg/dL is the target level for special high-risk populations. In the PROVE-IT study, a subgroup analysis showed less benefit in patients over the age of 65 compared with patients less than 65 years of age. The TNT trial excluded patients over the age of 75. Hence, the applicability of these data to the elderly population needs to be better defined. Optimal implementation of the current guidelines and the use of available agents will ultimately depend on expanding the knowledge base of healthcare providers, and may require far-reaching educational programs that change the way that risk-factor management is viewed by caregivers and patients alike.

Table 1. Categories of Risk and LDL-C Goals

Risk Category	0-1 Risk Factor	2+ Risk Factors
(10-Year Risk \leq 20%)	CHD or	CHD Risk Equivalents
(10-Year Risk $>$ 20%)		
LDL goal (mg/dL)	$<$ 160	$<$ 130
(Optional $<$ 100)	$<$ 100	
(Optional $<$ 70)		
LDL level at which to start TLC (mg/dL)	\leq 160	\leq 130
LDL level at which to consider drug therapy (mg/dL)	\leq 190	
(160-189: LDL-C lowering drug optional)	If 10-year risk is 10% to 20%, \leq 130	
If 10-year risk is $<$ 10%,	\leq 160	\leq 130 (100-129: LDL-C lowering drug optional)

CHD = coronary heart disease; LDL-C = low-density lipoprotein cholesterol; TLC = therapeutic lifestyle changes

Table adapted from: Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment

Panel III). JAMA. 2001;285:2486–2497

Table 2. Primary and Secondary Prevention Trials Involving Statin Therapy

Primary Prevention	Secondary Prevention
WOSCOPS[22]	CARE[24]
AFCAPS/TexCAPS[23]	LIPID[25]
HPS[10]	HPS[10]
ASCOT–LLA[11]	4S[26]
PROSPER[12]	
PROVE–IT[14]	
TNT[15]	

WOSCOPS = West of Scotland Coronary Prevention Study; AFCAPS/TexCAPS = Air Force/Texas Coronary Atherosclerosis Prevention Study; HPS = Heart Protection Study; ASCOT–LLA = Anglo–Scandinavian Cardiac Outcomes Trial – Lipid Lowering Arm; CARE = Cholesterol and Recurrent Events; LIPID = Long–Term Intervention with Pravastatin in Ischaemic Disease; 4S = Scandinavian Simvastatin Survival Study; PROSPER = Prospective Study of Pravastatin in the Elderly at Risk; PROVE–IT = Pravastatin or Atorvastatin and Infection Therapy; TNT = Treating to New Targets

Table 3. Effect of Simvastatin on Cardiovascular End Points by Patient Age

End Point	Reduction (%)
Age < 65	Reduction (%)
Age 65–70	
All–cause mortality	28 34
CAD mortality	42 43
Major coronary events	34 34
Coronary revascularization	35 41
Nonfatal MI	33 33
Any atherosclerosis–related point	24 34

CAD = coronary artery disease; MI = myocardial infarction

References

- 1.. Corti MC, Guralnik JM, Salive ME, et al. Clarifying the direct relation between total cholesterol levels and death from coronary heart disease in older persons. *Ann Intern Med.* 1997;126:753–760. Abstract
- 2.. Weijenberg MP, Feskens EJ, Kromhout D. Total and high density lipoprotein cholesterol as risk factors for coronary heart disease in elderly men during 5 years of follow-up. The Zutphen Elderly Study. *Am J Epidemiol.* 1996;143:151–158. Abstract
- 3.. Snowdon DA, Phillips RL, Fraser GE. Meat consumption and fatal ischemic heart disease. *Prev Med.* 1984;13:490–500. Abstract
- 4.. Low incidence of assessment and modification of risk factors in acute care patients at high risk for cardiovascular events, particularly among females and the elderly. The Clinical Quality Improvement Network (CQIN) Investigators. *Am J Cardiol.* 1995;76:570–573. Abstract
- 5.. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA.* 2001;285:2486–2497. Abstract
- 6.. Denke MA, Grundy SM. Hypercholesterolemia in elderly persons: resolving the treatment dilemma. *Ann Intern Med.* 1990;112:780–792. Abstract
- 7.. Hulley SB, Rosenman RH, Bawol RD, Brand RJ. Epidemiology as a guide to clinical decisions. The association between triglyceride and coronary heart disease. *N Engl J Med.* 1980;302:1383–1389. Abstract
- 8.. Austin MA, Hokanson JE, Edwards KL. Hypertriglyceridemia as a cardiovascular risk factor. *Am J Cardiol.* 1998;81:7B–12B. Abstract
- 9.. Assmann G, Schulte H, Funke H, von Eckardstein A. The emergence of triglycerides as a significant independent risk factor in coronary artery disease. *Eur Heart J.* 1998;19(supplM):M8–14.
- 10.. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet.* 2002;360:7–22. Abstract
- 11.. Sever PS, Dahlof B, Poulter NR, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial -- Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *Lancet.* 2003;361:1149–1158. Abstract
- 12.. Shepherd J, Blauw GJ, Murphy MB, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. *Lancet.* 2002;360:1623–1630. Abstract
- 13.. Grundy SM, Cleeman JI, Merz CN, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation.* 2004;110:227–239. Abstract
- 14.. Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med.* 2004;350:1495–1504. Abstract
- 15.. LaRosa JC, Grundy SM, Waters DD, et al; Treating to New Targets (TNT) Investigators. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med.* 2005;352:1425–1435. Abstract

- 16.. de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation*. 1999;99:779–785. Abstract
- 17.. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med*. 2003;348:2599–2608. Abstract
- 18.. Knoop KT, de Groot LC, Kromhout D, et al. Mediterranean diet, lifestyle factors, and 10–year mortality in elderly European men and women: the HALE project. *JAMA*. 2004;292:1433–1439. Abstract
- 19.. Lemaitre RN, King IB, Mozaffarian D, Kuller LH, Tracy RP, Siscovick DS. n–3 Polyunsaturated fatty acids, fatal ischemic heart disease, and nonfatal myocardial infarction in older adults: the Cardiovascular Health Study. *Am J Clin Nutr*. 2003;77:319–325. Abstract
- 20.. Fletcher GF, Balady G, Blair SN, et al. Statement on exercise: benefits and recommendations for physical activity programs for all Americans. A statement for health professionals by the Committee on Exercise and Cardiac Rehabilitation of the Council on Clinical Cardiology, American Heart Association. *Circulation*. 1996;94:857–862. Abstract
- 21.. Takemoto M, Liao JK. Pleiotropic effects of 3–hydroxy–3–methylglutaryl coenzyme a reductase inhibitors. *Arterioscler Thromb Vasc Biol*. 2001;21:1712–1719. Abstract
- 22.. Shepherd J, Cobbe SM, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. West of Scotland Coronary Prevention Study Group. *N Engl J Med*. 1995;333:1301–1307. Abstract
- 23.. Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. *JAMA*. 1998;279:1615–1622. Abstract
- 24.. Sacks FM, Pfeffer MA, Moya LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. *N Engl J Med*. 1996;335:1001–1009. Abstract
- 25.. Hunt D, Young P, Simes J, et al. Benefits of pravastatin on cardiovascular events and mortality in older patients with coronary heart disease are equal to or exceed those seen in younger patients: results from the LIPID trial. *Ann Intern Med*. 2001;134:931–940. Abstract
- 26.. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet*. 1994;344:1383–1389. Abstract
- 27.. Miettinen TA, Pyorala K, Olsson AG, et al. Cholesterol–lowering therapy in women and elderly patients with myocardial infarction or angina pectoris: findings from the Scandinavian Simvastatin Survival Study (4S). *Circulation*. 1997;96:4211–4218. Abstract
- 28.. Pacala JT, McBride PE, Gray SL. Management of older adults with hypercholesterolemia. *Drugs Aging*. 1994;4:366–378. Abstract
- 29.. Santinga JT, Rosman HS, Rubenfire M, et al. Efficacy and safety of pravastatin in the long–term treatment of elderly patients with hypercholesterolemia. *Am J Med*. 1994;96:509–515. Abstract
- 30.. Hulley SB, Newman TB. Cholesterol in the elderly. Is it

important? JAMA. 1994;272:1372–1374.

31.. Rubins HB, Robins SJ, Collins D, et al. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. N Engl J Med. 1999;341:410–418. Abstract

32.. Carlson LA, Rosenhamer G. Reduction of mortality in the Stockholm Ischaemic Heart Disease Secondary Prevention Study by combined treatment with clofibrate and nicotinic acid. Acta Med Scand. 1988;223:405–418. Abstract

33.. Van Heek M, Farley C, Compton DS, Hoos L, Davis HR. Ezetimibe selectively inhibits intestinal cholesterol absorption in rodents in the presence and absence of exocrine pancreatic function. Br J Pharmacol. 2001;134:409–417. Abstract

34.. Van Heek M, France CF, Compton DS, et al. In vivo metabolism-based discovery of a potent cholesterol absorption inhibitor, SCH58235, in the rat and rhesus monkey through the identification of the active metabolites of SCH48461. J Pharmacol Exp Ther. 1997;283:157–163. Abstract

35.. Feldman T, Koren M, Insull W Jr, et al. Treatment of high-risk patients with ezetimibe plus simvastatin co-administration versus simvastatin alone to attain National Cholesterol Education Program Adult Treatment Panel III low-density lipoprotein cholesterol goals. Am J Cardiol. 2004;93:1481–1486. Abstract

36.. Kannel WB. Importance of hypertension as a major risk factor in cardiovascular disease. In: Bosch JGR, ed. Hypertension. New York: McGraw-Hill; 1999:888–910.

Tarek Helmy, MD, Assistant Professor of Medicine and Cardiology, Grady Memorial Hospital, Atlanta, Georgia. Email: thelmy@xxxxxxxxxx

Amar D. Patel, MD, Cardiology Fellow, Division of Cardiology, Emory University School of Medicine, Atlanta, Georgia

Fadi Alameddine, MD, Fellow, Interventional Cardiology, Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia

Nanette K. Wenger, MD, FACC, FAHA, Chief of Cardiology, Grady Memorial Hospital, Atlanta, Georgia; Professor of Medicine, Department of Medicine, Division of Cardiology, Emory University School of Medicine, Atlanta, Georgia

Disclosure: Tarek Helmy, MD, has disclosed no relevant financial relationships.

Disclosure: Amar D. Patel, MD, has disclosed no relevant financial relationships.

Disclosure: Fadi Alameddine, MD, has disclosed no relevant financial relationships.

Disclosure: Nanette K. Wenger, MD, FACC, has disclosed that she has received research grants/contracts from and is on the trial steering committee for Eli Lilly, AstraZeneca, and Pfizer, and is a consultant for the Eli Lilly Raloxifene Advisory Committee; Heart Disease in Women, MED-ED; Pfizer; the Cardiology/Lipidology Advisory Board, Merck; Bristol-Myers Squibb; the Ranolazine Advisory Board, CV Therapeutics; Sanofi-Aventis; Kos Pharmaceuticals W.A.T.C.H. Program; the NitroMed Heart Failure Advisory Board; Leadership Council for Improving Cardiovascular Care Executive Committee; Schering-Plough; and the Coreg Post-MI Advisory Panel, GlaxoSmithKline. Dr. Wenger has also disclosed that she is on the speaker's bureau (CME) for Pfizer, Novartis, Merck, Bristol-Myers Squibb, Eli Lilly, and NitroMed.

```
begin 666 spacer.gif
K1TE&.#EA`0`!( `~~~~~"Y! $~~~~+ ~~~~!`$~~~("1 $`.P`
`
end
```

```
begin 666 spacer.gif
K1TE&.#EA`0`!( `~~~~~"Y! $~~~~+ ~~~~!`$~~~("1 $`.P`
`
end
```

.

-
- Prev by Date: **[Re: atenolol user take note:](#)**
 - Next by Date: **[Re: Lawsuit questions need for Lipitor: The ASCOT trial's 2000 women](#)**
 - Previous by thread: **[Can Low Cholesterol Increase Your Parkinson's Risk?](#)**
 - Next by thread: **[advisories on fish consumption & mercury may do more harm than good](#)**
 - Index(es):
 - ◆ **[Date](#)**
 - ◆ **[Thread](#)**