

## 2013 American College of Cardiology/American Heart Association Guidelines on Treatment of Hypercholesterolemia

Wilbert S Aronow\*

Cardiology Division, Department of Medicine, Westchester Medical Center/New York Medical College, Valhalla, New York, USA

High-dose statins reduce serum low-density lipoprotein (LDL) cholesterol  $\geq 50\%$  and include atorvastatin 40 mg to 80 mg daily and rosuvastatin 20 mg to 40 mg daily [1]. Moderate-dose statins reduce serum LDL cholesterol 30% to 49% and include atorvastatin 10 mg to 20 mg daily, rosuvastatin 5 mg to 10 mg daily, simvastatin 20 mg to 40 mg daily, pravastatin 40 mg to 80 mg daily, lovastatin 40 mg daily, fluvastatin XL 80 mg daily, fluvastatin 40 mg twice daily, and pitavastatin 2mg to 4 mg daily [1]. Low-dose statins reduce serum LDL cholesterol less than 30% and include simvastatin 10 mg daily, pravastatin 10 mg to 20 mg daily, lovastatin 20 mg daily, fluvastatin 20 mg to 40 mg daily, and pitavastatin 1 mg daily [1].

The 2013 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines on treatment of hypercholesterolemia state that lifestyle modification must be used both prior to cholesterol-lowering drug therapy and together with use of cholesterol-lowering drug therapy [1]. Lifestyle modification includes a heart healthy diet, regular exercise, avoidance of tobacco products, and an ideal body weight [1].

These guidelines support the use of statins in 4 major groups [1]. Group 1 is persons who have clinical evidence of atherosclerotic cardiovascular disease (ASCVD). ASCVD includes acute coronary syndromes, a history of myocardial infarction, stable or unstable angina pectoris, coronary or other arterial revascularization, stroke, transient ischemic attack, or atherosclerotic peripheral arterial disease [1]. These guidelines recommend use of high-dose statins in men and in women aged 75 years and younger with clinical evidence of ASCVD with a class I indication. If high-dose statins are associated with adverse effects in patients with ASCVD, moderate-dose statins are recommended if tolerated with a class I indication. In patients older than 75 years with clinical ASCVD, use of high-dose or moderate-dose statins has a class IIa indication [1].

Patients with New York Heart Association class II, III, or IV heart failure and patients undergoing maintenance hemodialysis are unlikely to benefit from treatment from statins. No recommendation was made regarding initiation or continuation of statin therapy in these patients [1].

The ACC/AHA guidelines state that persons with a serum LDL cholesterol  $\geq 190$  mg/dL or serum triglycerides  $\geq 500$  mg/dL should be investigated for secondary causes of hyperlipidemia. Secondary causes of increased serum LDL cholesterol include dietary saturated or trans fats, weight gain, anorexia, diuretics, cyclosporine, glucocorticoids, amiodarone, biliary obstruction, nephrotic syndrome, hypothyroidism, obesity, and pregnancy [1]. Use of statins, niacin, and ezetimibe are contraindicated during pregnancy and lactation.

Secondary causes of hypertriglyceridemia include weight gain, very low-fat diets, high intake of refined carbohydrates, excessive alcohol intake, oral estrogens, glucocorticoids, bile acid sequestrants, protease inhibitors, retinoic acid, anabolic steroids, sirolimus, raloxifene, tamoxifen, beta blockers (not carvedilol), thiazides, nephrotic syndrome, chronic renal failure, lipodystrophies, hypothyroidism, obesity, and pregnancy [1].

The ACC/AHA guidelines recommend treating persons aged 21 years and older with a serum LDL cholesterol  $\geq 190$  mg/dL (group 2) with high-dose statins with a class I indication. For persons unable to tolerate high-dose statins, use the maximum tolerated dose of statin [1].

The ACC/AHA guidelines recommend for primary prevention in persons with diabetes mellitus and a serum LDL cholesterol between 70 to 189 mg/dL (group 3) moderate-dose statins in adults aged 40 to 75 years of age with a class I indication [1]. If the 10-year risk of ASCVD is  $\geq 7.5\%$  using the Pooled Cohort Equations [2,3], high-dose statins is reasonable in diabetics aged 40 to 75 years with a class IIa indication [1]. In diabetics younger than 40 years and older than 75 years, moderate-dose statins or high-dose statins is reasonable to use with a class IIa indication [1].

The Pooled Cohort Equations [2,3] should be used to estimate the 10-year ASCVD risk in persons with a serum LDL cholesterol between 70 to 189 mg/dL without ASCVD or diabetes mellitus [1]. Sex, age, race, serum total cholesterol, serum high-density lipoprotein (HDL) cholesterol, systolic blood pressure, treatment for hypertension, diabetes mellitus, and smoking are the variables used to estimate the 10-year risk of ASCVD.

Persons aged 40 to 75 years with a serum LDL cholesterol of 70 to 189 mg/dL without ASCVD or diabetes mellitus and an estimated 10-year ASCVD risk of  $\geq 7.5\%$  (group 4) should be treated with high-dose or moderate-dose statins with a class I indication [1]. It is reasonable to treat persons aged 40 to 75 years with a serum LDL cholesterol of 70 to 189 mg/dL without ASCVD or diabetes mellitus and an estimated 10-year ASCVD risk of 5% to 7.4% with moderate-dose statins [1].

Besides the use of statins in these 4 groups, other factors may be considered in consideration of statin therapy. These factors include a primary serum LDL cholesterol of  $\geq 160$  mg/dL or other evidence of genetic hyperlipidemia, a family history of premature ASCVD with onset before age 55 years in a first-degree male relative, onset before age 65 years in a first-degree female relative, high-sensitivity C-reactive protein  $\geq 2$  mg/L, a coronary calcium score  $\geq 300$  Agaston units or  $\geq 75$  percentile for age, sex, and ethnicity, an ankle-brachial index less than 0.9, or an increased lifetime risk of ASCVD [1].

\*Corresponding author: Wilbert S. Aronow, MD, FACC, FAHA, Cardiology Division, New York Medical College, Macy Pavilion, Room 138, Valhalla, NY 10595, USA, Tel: (914) 493-5311; Fax: (914) 235-6274; E-mail: [wsaronow@aol.com](mailto:wsaronow@aol.com)

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Bile acid sequestrants should not be used in persons with fasting serum triglycerides  $\geq 300$  mg/dL or type III hyperlipoproteinemia because severe triglyceride increases may occur (class III indication harm) [1]. Gemfibrozil is contraindicated in patients treated with statins (class III indication harm). Fenofibrate may be considered in patients on low-dose statins or moderate-dose statins with serum triglycerides  $\geq 500$  mg/dL with a class IIb indication [1]. Fenofibrate is contraindicated in these patients if the estimated glomerular filtration rate is less than 30 mL/minute/1.73 m<sup>2</sup> (class III indication harm) [1]. If the the estimated glomerular filtration rate is between 30 and 59 mL/minute/1.73 m<sup>2</sup>, the fenofibrate dose should not exceed 54 mg/day [1]. If omega-3 fatty acids are used for the treatment of serum triglycerides  $\geq 500$  mg/dL, the patient should be evaluated for gastrointestinal disturbances, skin changes, and bleeding [1].

The ACC/AHA guidelines committee also found no evidence that titration of statins or combination drug therapy to achieve specific LDL cholesterol levels or non-HDL cholesterol levels or percent decrease improved ASCVD outcomes. Therefore, the guidelines do not recommend their use as performance measures [1]. In the AIM-High trial (Atherothrombosis Intervention in Metabolic Syndrome With Low HDL/High Triglycerides and Impact on Global Health Outcomes), the additional decrease in non-HDL cholesterol as well

as additional decreases in Apo B, Lp(a), and triglycerides in addition to increases in HDL cholesterol levels in patients treated with niacin therapy in addition to simvastatin did not reduce ASCVD risk and insignificantly increased stroke 61% (p=0.11) [1,4].

## Declaration

The author has no conflicts of interest.

## References

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