REVIEW ARTICLE

Update on the Role of Statins in the Prevention of Atherosclerotic Cardiovascular Disease

Kimberly A. B. Cauthon, PharmD, CGP,[1] Erin Raney, PharmD, BCPS, BC-ADM,[2] and Shannon C. Scott, DO[3]

[1]Feik School of Pharmacy, University of the Incarnate Word, San Antonio, Texas
[2]College of Pharmacy-Glendale, Midwestern University, Glendale, Arizona
[3]Arizona College of Osteopathic Medicine, Midwestern University, Glendale, Arizona

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The treatment of dyslipidemia is evolving. New guidelines from the American College of Cardiology (ACC)/American Heart Association (AHA) and National Lipid Association (NLA) have brought changes to the previous standards of care. The ACC/AHA update no longer suggests treating to specific cholesterol goals, a new atherosclerotic cardiovascular disease assessment has been recommended, and treatment recommendations are divided into four statin benefit groups. The ACC/AHA focuses their update on lipid lowering therapy shown in clinical trials to provide long term cardiovascular risk reduction. The ACC/AHA and NLA guidelines are in agreement with statins as the chosen primary treatment but NLA guidelines continue to recommend treatment to specific LDL-C goals and stratify atherosclerotic cardiovascular disease (ASCVD) risk by number of risk factors and other conditions. The four statin treatment groups advised by the ACC/AHA update are patients with ASCVD, patients with primary elevation of LDL-C ≥ 190 mg/dL, patients with diabetes ages 40 to 75 years with LDL-C 70 to 189mg/dL, and patients without ASCVD or diabetes with an estimated 10-year ASCVD risk ≥ 7.5%. Due to the lack of clinical trial data in certain populations, the ACC/AHA guidelines outline fewer recommendations for younger patients, debate statin intensity choice in patients with diabetes, and provide less support for statin use in elderly patients. ASCVD risk should be evaluated in all adult patients. Risks and benefits of treatment should be considered with respect to patient preferences regarding therapy.

INTRODUCTION

As heart disease and stroke remain leading causes of death in the United States, there is a continued focus on improving the treatment of dyslipidemia as a major risk factor.[1,2] An update to the previous National Heart, Lung, and Blood Institute (NHLBI) lipid guidelines (National Cholesterol Education Program Adult Treatment Panel III) published in 2002 and updated in 2004 had been anticipated in 2013.[3,4] In place of these guidelines, the American College of Cardiology (ACC) and the American Heart Association (AHA) collaborated with the NHLBI to publish guidance documents for the assessment of cardiovascular risk, lifestyle modifications to reduce cardiovascular risk, management of blood cholesterol in adults, and management of overweight and obesity in adults.[5] The ACC/AHA guidelines focus on the prevention of atherosclerotic cardiovascular disease (ASCVD) and are not intended as a comprehensive treatment strategy for dyslipidemia.[5]

The National Lipid Association (NLA) followed the ACC/AHA with a recent publication of guidelines addressing cholesterol screening and classification in adults, ASCVD risk assessment and treatment goals, and drug therapies intended to reduce morbidity and mortality.[6] The second part of the report is currently in development and will address lifestyle recommendations, groups with special considerations, patient adherence strategies, and team-based collaborative care. The NLA guidelines are intended to represent a comprehensive patient care approach that is similar to that provided by the prior NHLBI-sponsored guidelines.[6]

There are several notable changes to the treatment recommendations in the ACC/AHA guidelines. The updates no longer suggest treating to specific cholesterol goals, and instead utilize drug therapies that provide lipid lowering shown in clinical trials to provide long term cardiovascular risk reduction.[5] The use of a new ASCVD risk assessment tool is the basis for treatment recommendations.[7] The estimated 10-year ASCVD risk is defined as first occurrence of non-fatal myocardial infarction (MI), coronary heart disease (CHD) death, and nonfatal and fatal stroke.

Assessment of ASCVD risk should occur every 4 to 6 years for patients ages 20 to 79.[5,7] It is easily calculated using sex-specific pooled cohort equations found at www.myamericanheart.org/cvriskcalculator.[8] For patients ages 20 to 39 or those at low 10-year risk, ages 40 to 59, a long-term or lifetime risk calculation is recommended.[7] This long-term risk can be easily calculated by using the Framingham Heart cardiovascular risk calculator

Address correspondence to: Kimberly A. B. Cauthon, PharmD, CGP, Assistant Professor, Department of Pharmacy Practice
Feik School of Pharmacy University of the Incarnate Word.
4301 Broadway, CPO #99 | San Antonio, Texas 78209
Phone: 210.883.1132 Fax: 210.822.1516 Email: cauthon@uiwtx.edu

found at www.framinghamheartstudy.org/risk-functions/cardiovascular-disease/10-year-risk.php.[6] These equations are well calibrated for non-Hispanic Whites and African Americans. They may overestimate ASCVD risk in American Indians and Asian Americans.[7] The ACC/AHA calculation also includes stroke risk where the Framingham does not. The NHLBI evidence grade for using the pooled cohort equations as the 10-year ASCVD risk calculator is E (expert opinion).[5] There has been much discussion regarding the accuracy of the ASCVD risk assessment tool.[9] Validation of efficacy has been published in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study in 2014.[10]

The treatment recommendations are divided into four "statin-benefit" groups based upon evidence from randomized controlled trials and meta-analyses published through July, 2013 (see Table 1).[5] Statin-based therapy is promoted as the primary pharmacotherapy choice, as clinical trial data do not support the use of non-statins in most individuals. Statins are recommended in fixed-doses to mimic clinical trials, rather than titrated (dose-adjusted) statins to achieve pre-specified low-density lipoprotein cholesterol (LDL-C) or non-LDL-C goals.[5]

In contrast, while the NLA guidelines recommend statins as the primary treatment for reducing ASCVD risk and recognize the value of fixed-dose statin therapy, they continue to recommend treatment to specific LDL-C goals and non-HDL-C goals.[6] The NLA states that treatment goals facilitate effective communication between patients and clinicians with objective, trackable outcome measures. Additionally, ASCVD risk is stratified by number of risk factors and other co-morbid conditions. The NLA risk assessment categories are low, moderate, high, and very high with a corresponding LDL-C goal of < 100mg/dL and non-HDL-C goal < 130mg/dL for all risk categories except an LDL-C goal of < 70mg/dL and non-HDL-C goal of < 100mg/dL for very high risk patients (i.e. patients with ASCVD). The threshold of high risk is ≥ 15% using the 10-year ASCVD risk assessment tool rather than ≥ 7.5% assigned by the ACC/AHA guidelines.[5, 6]

This review will focus on three patient cases commonly encountered in primary care settings where the ACC/AHA recommendations are in debate or limited. In addition, it will provide the NLA's position regarding the cases where appropriate. Case one examines risk assessment and primary prevention, case two considers statin choices in a patient with diabetes, and case three highlights treatment decisions in an elderly patient.

TABLE 1:

ACC / AHA Recommended "Statin-Benefit" Groups [5]

Statin Treatment Group	Recommended Statin Intensity	Level of Evidence *
1. Secondary prevention in patients with Clinical ASCVD	High-intensity for patients ≤ 75 years of age	A
	Moderate-intensity for patients > 75 years of age	A
2. Primary prevention in patients with primary elevations of LDL-C ≥ 190 mg/dL	High-intensity for patients ≥ 21 years of age	B
3. Primary prevention in individuals with diabetes 40 – 75 years of age and LDL-C 70-189mg/dL	Moderate-intensity	A
	High-intensity when ≥ 7.5% 10-year ASCVD risk	B
4. Primary prevention in individuals without diabetes ages 40-75 with an estimated 10-year ASCVD risk ≥ 7.5%, and LDL-C 70-189 mg/dL	Moderate or high-intensity	A

* Level of evidence "A" recommendations are derived from multiple randomized clinical trials and meta-analyses. Level of evidence "B" recommendations stem from single randomized trials or nonrandomized studies.[5]

CASE 1

A 36 year old African American female presents for her annual physical exam. She has no significant past medical history. Her father died from a myocardial infarction at age 50. She has smoked 1 pack of cigarettes per day for the past 10 years. She works as an administrative assistant and walks 20 minutes for exercise two times per week. Her blood pressure is 135/80mmHg and her BMI is 30kg/m^2. The results of her fasting lipid panel are: total cholesterol 200mg/dL, LDL-C 140mg/dL, HDL-C 50mg/dL, and non-HDL-C 150mg/dL. Her fasting blood glucose is 95mg/dL and A1C is 6.2%. What is the best approach to assess her ASCVD risk?

For this 36 year old woman, her major ASCVD risks include smoking and premature CHD in her father (see Figure 1). Her lifetime ASCVD risk totals 39% using the 10-year ASCVD risk calculator.[5, 7, 8] Her 30-year risk of ASCVD is 22%.[6]

The ACC/AHA guidelines recommend drug therapy for dyslipidemia in this age group (20 to 39 years) depending upon the patient's risk factors, preferences, and clinician's judgement.[5] In comparison, the NLA assigns a "high risk" designation to a 30-year ASCVD risk ≥ 45% in any patient with diabetes or ASCVD equivalents.[6] This patient has 2 major ASCVD risk factors and is determined by NLA standards to be at "moderate risk."[6] The NLA goals for moderate risk groups include non-HDL-C < 130mg/dL and LDL-C < 100mg/dL.[6] As mentioned previously, the ACC/AHA guidelines do not support cholesterol targets for any age group. However, a trial of lifestyle changes in low to moderate ASCVD groups is supported by both guidelines before starting drug therapy.

Recommended lifestyle changes include a reduction of saturated fat and cholesterol, smoking cessation, moderate to vigorous physical activity 45 minutes three times per week, weight loss, and referral to a registered dietician.[11]

FIGURE 1:

Major ASCVD Risk Factors [6]

- **Age** (male ≥ 45 years or female ≥ 55 years)
- **Family history of early coronary heart disease (CHD) in a first degree relative** (< 55 years male or < 65 years female)
- **Low HDL-C** (< 40mg/dL male or < 50mg/dL female)
- **High blood pressure** (≥ 140 / ≥ 90 or on blood pressure medications)
- **Current smoking**

At this patient's visit, lifestyle changes are emphasized, with a focus on smoking cessation and heart-healthy diet choices. After 3 months if cholesterol levels have not decreased despite lifestyle modifications, drug therapy is recommended for non-HDL-C ≥ 160mg/dL or LDL-C ≥ 130mg/dL.[6]

After following this patient for 5 years, she returns at age 41. She is now smoking ½ pack per day and is treated with hydrochlorothiazide for hypertension. Her current BMI is 32kg/m^2 and her blood pressure is 136/86mmHg. The results of her fasting lipid panel are: total cholesterol 260mg/dL, LDL-C 165mg/dL, HDL-C 35mg/dL, non-HDL-C 225mg/dL. Her A1C is 6.0%. Her liver function tests are in the normal range. What is the best approach to her cardiovascular risk assessment at this stage?

Since the ACC/AHA guidelines and the NLA recommend a 10-year risk calculation for patients 40 to 79 years without ASCVD, her 10-year ASCVD risk is 15.1% and 30-year risk is now 50% (increased from 39%).[8] According to the Framingham risk calculation, her 10-year risk is 14%.[6] In addition to lifestyle changes, a moderate to high intensity statin should be considered because her 10-year ASCVD risk is ≥ 7.5% and she has 3 or more major ASCVD risk factors (smoking, hypertension, family history of premature CHD, and HDL < 50 mg/dL in a female).[5-7]

Critical discussion points at this time include risks and benefits of statin treatment and patient preferences as well as a continued focus on the benefits of managing her other risk factors. For example, if she quit smoking, her ASCVD 10-year risk would decrease to 7.9%.[8] According to a Cochrane review of statins for primary prevention, drug therapy was shown to reduce all-cause mortality in patients with no history of ASCVD. They report "of 1,000 people treated with a statin for five years, 18 would avoid a major CVD event." Statins are cost effective and do not increase the risk of serious adverse effects.[12] This patient does not have characteristics commonly associated with statin adverse effects (see Figure 2). She is, however, at risk for diabetes given an A1C that suggests insulin resistance.[13]

Extended use of moderate intensity statin therapy may be associated with diabetes.[14-16] The diabetes risk with moderate intensity statins is lower than with high intensity statins and since she has such a high ASCVD risk, the benefits of preventing ASCVD likely outweigh the risks of diabetes. After a thorough discussion, she agrees to start a moderate intensity statin. When choosing a statin for her, the expected potency (dose-related lipid lowering effect) guides treatment decisions.[5] A moderate intensity statin usually lowers LDL-C by 30-49% and a high intensity statin usually lowers LDL-C by ≥ 50%. See Table 2 for a comparison of moderate and high

intensity statins. This patient should be started at the target statin dose. It is not recommended to titrate up in a stepwise fashion. Her next lipid panel should be performed in 4 to 12 weeks to assess adherence. Future lipid panels should be assessed in 3 to 12 months based on clinical judgment.

FIGURE 2:

Characteristics Associated with Statin Adverse Effects [5]

- **Multiple comorbidities**
- **Impaired renal or hepatic function**
- **History of muscle disorders**
- **History of statin intolerance**
- **Concomitant use of medications known to impact statin metabolism**
- **History of hemorrhagic stroke**
- **> 75 years**

TABLE 2:

Statin Doses and Intensity [5]

Statin^	Moderate - Intensity Daily Dose	High - Intensity Daily Dose
Atorvastatin	10 - 20 mg	40 - 80 mg
Fluvastatin	40 mg twice daily	
Lovastatin	40 mg	
Pitavastatin	2 - 4 mg	
Pravastatin	40 - 80 mg	
Rosuvastatin	5 - 10 mg	20 - 40 mg
Simvastatin	20 - 40 mg*	

^ Statins Used in RCTs: Chart modified from the 2014 NLA consensus set of recommendations for dyslipidemia and 2013 ACC/AHA guidelines on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults

*Initiation of Simvastatin 80 mg is not recommended by the FDA because of the risk of myopathy.

CASE 2

A 58 year old Caucasian male presents quarterly for his Type 2 diabetes visit at a family medicine clinic. Other medical conditions include hypertension and dyslipidemia. He has no history of ASCVD. His medications include simvastatin 40mg at bedtime for the past five years, lisinopril 40mg daily, amlodipine 10mg daily, aspirin 81mg daily, metformin 1000mg twice daily, and insulin glargine 15 units daily. He denies tobacco or alcohol use. His blood pressure is 128/74mmHg and BMI is 33kg/m^2. The results of his fasting lipid panel are: total cholesterol 205mg/dL, LDL-C 90mg/dL, HDL-C 32mg/dL, and triglycerides 411mg/dL. A previous lipid panel is not available. The fasting blood glucose is 180mg/dL, and A1C is 10.2%. What is the best approach to address his statin therapy?

Cardiovascular disease is a major cause of morbidity and mortality in patients with diabetes.[13] The AHA/ACC guidelines recommend a moderate or high intensity statin for patients with diabetes.[5] This patient is currently receiving a moderate-intensity statin. To determine the optimal statin dosing, his current LDL-C and triglyceride levels should be considered, along with potential and current drug interactions. The ACC/AHA guidelines recommend a moderate intensity statin for primary prevention for patients with diabetes ages 40 to 75 years with an LDL-C 70 to 189mg/dL.[5] A high intensity statin is recommended when the 10-year ASCVD risk is ≥ 7.5%, although the evidence supporting this is weaker. The level of evidence is B that is derived from single randomized trials or nonrandomized studies.[5] There are no large randomized control trials in patients with diabetes that compare high intensity and low intensity statins. An additional management challenge surfaces as the 10-year ASCVD risk calculator is not intended for use in patients already taking a statin.[7]

The NLA guidelines for treatment in patients with diabetes recommend a moderate to high intensity statin irrespective of the baseline LDL-C level due to the designation of diabetes as a high or very high ASCVD risk group.[6] An LDL-C goal ≤ 100mg/dL is recommended for those with diabetes and 0 to 1 other major ASCVD risk factors as long as there is no evidence of end organ damage (defined as an albumin/creatinine ratio of ≥ 30mg/g, chronic kidney disease (CKD), or retinopathy). An LDL-C goal < 70mg/dL is recommended where there are at least two ASCVD risk factors or evidence of end organ damage. This patient has at least three risk factors: age ≥ 45 years, high blood pressure treated with medication, and low HDL-C. The American Diabetes Association (ADA) updated their standards of care to mirror the ACC/AHA guidelines.[13] For patients already on a statin in whom the baseline LDL-C is unknown, statin

trials reported that LDL-C < 100mg/dL was observed in most individuals receiving high-intensity statins.

Hypertriglyceridemia is common in patients with Type 2 diabetes, with approximately 35% having triglyceride (TG) levels ≥ 200mg/dL.[17] Elevated TG levels are typically associated with low HDL-C and small dense LDL-C particles. Type 2 diabetes can cause increased hepatic VLDL-C production due to insulin resistance.[17] The ACC/AHA and NLA guidelines classify TG as high (200-499mg/dL) and very high (≥ 500mg/dL).[5, 6] TG do not become the target for primary treatment until ≥ 500mg/dL to reduce the risk of pancreatitis. However, it is not clear if there are cardiovascular benefits related to treating TG below this cutpoint. The Endocrine Society has a different classification system and classifies hypertriglyceridemia as moderate (200-999mg/dL), severe (1,000-1,999mg/dL), and very severe (≥ 2,000mg/dL).[18]

Treatment of hypertriglyceridemia in the moderate range can include statins.[5] The use of fibric acid derivatives is not recommended until TG are > 999mg/dL per the Endocrine Society.[18] The use of fibric acids, niacin, or omega-3 fatty acids are recommended for management of TG > 499mg/dL per the ACC/AHA and NLA guidelines.[5, 6] Gemfibrozil should not be initiated in patients on statin therapy given the risk for myopathy and rhabdomyolysis.[5] Gemfibrozil inhibits glucuronidation which is an elimination pathway of all the statins and increases the risk of adverse effects.[19]

TABLE 3:

Simvastatin Drug Interactions [23]

Simvastatin Maximum Dose with Concomitant Medication	Concomitant Medication
10 mg	Verapamil Diltiazem Dronedarone
20 mg	Amiodarone Amlodipine Ranolazine
Contraindicated	Strong CYP3A4 Inhibitors, e.g.: Itraconazole, Ketoconazole, Posaconazole, Voriconazole Erythromycin, Clarithromycin, Telithromycin HIV protease inhibitors Boceprevir, Telaprevir Cyclosporine Grapefruit juice

Fenofibrate may be considered concomitantly with a low or moderate intensity statin if TG are ≥ 500mg/dL.[5] A recent systematic review from the Agency for Healthcare Research and Quality (AHRQ) found non-statin and statin combinations can further decrease LDL-C but no studies demonstrate additional benefit for ASCVD mortality.[20] Combination therapy is therefore not recommended for the purpose of decreasing ASCVD risk.[5] Statins should be recommended at the maximum dose tolerated before adding another drug for TG.[6] It is important to note that according to the manufacturer's product labeling, atorvastatin 40mg and 80mg daily doses can reduce TG by 29% and 37%, respectively.[21] Additionally, rosuvastatin 20mg and 40mg daily doses can lower TG by 23% to 28%.[22]

Statins vary in their drug interactions through different mechanisms in metabolism.[19] Simvastatin and lovastatin have more drug interactions since they are substrates of the cytochrome p450 3A4 pathway. Atorvastatin is a substrate for cytochrome p450 3A4 enzymes but other available routes of metabolism limit the extent of its drug interactions. Rosuvastatin, pitavastatin, fluvastatin, and pravastatin have the lowest propensity towards drug interactions.[19] The drug interactions for simvastatin are listed in Table 3.

To make a final decision regarding this patient's optimal statin dosing, his current LDL-C and TG must be considered along with his potential for drug-drug interactions. Since a baseline LDL-C is unavailable, an accurate 10-year ASCVD risk score cannot be calculated.[7] Per the NLA, the patient should have further LDL-C lowering since he is not at the goal of less than 70mg/dL and per the ACC/AHA, a higher intensity statin could be considered.[5, 6] The patient's TG are moderate to high but not greater than 500mg/dL and can be further reduced with better blood glucose control and a higher intensity statin. Because the maximum dose of simvastatin in combination with amlodipine is 20mg daily, the patient is considered to be at higher risk of drug-drug interactions and adverse effects with his dose of simvastatin 40mg daily.[23] This interaction is based on pharmacokinetic studies.[24] Considering our patient's LDL-C, TG, and current drug-drug interaction, the simvastatin 40mg should be changed to atorvastatin 40mg daily or rosuvastatin 20mg daily to achieve maximal benefits with limited safety concerns.

CASE 3

A 77 year old Caucasian male newly establishes with a family physician after moving to the area. He has a history of benign prostatic hyperplasia and hypertension, managed with tamsulosin 0.4mg once daily and lisinopril 10mg once daily. He denies family history of cardiovascular disease. He reports no tobacco use for 14 years; he previously smoked 1 pack of

cigarettes per day for 45 years. His BMI is 32.6kg/m^2 and his blood pressure is 138/88mmHg. The results of his fasting lipid panel are: total cholesterol 221mg/dL, HDL-C 37mg/dL, LDL-C 150mg/dL, non-HDL-C 184mg/dL. The high-sensitivity C-reactive protein is 4.4mg/dL, and his comprehensive metabolic panel is within normal limits. What is the best approach to this patient's cardiovascular risk assessment and treatment?

As stated previously, the 10-year ASCVD risk calculator is validated for use in adults between the ages of 21 and 79. Based upon the data provided, this patient has an estimated 10-year ASCVD risk of 38.9%.[8] The ACC/AHA guidelines refer to the use of the 10-year risk assessment to identify statin benefit groups up to the age of 75 years.[5] This age cut point is related to the lack of clinical trial data supporting positive clinical outcomes in older age cohorts and the tendency towards a higher risk of statin-related adverse effects from drug-drug interactions and comorbidities. If the patient was younger than 75, his 10-year ASCVD risk would clearly support initiation of a statin (7.5% or higher). However, his age of 77 falls outside these parameters.

In situations of uncertainty, a patient's need for primary versus secondary cardiovascular prevention can provide clarification. For example, in the setting of secondary prevention for patients older than 75 years with clinical ASCVD, the guidelines support statin therapy but at a moderate-intensity level rather than the high-intensity statin recommended for the younger patient.[5] For primary prevention, consideration of other risk factors can facilitate decision making (see Figure 3). Notably, the guidelines do support continuation of chronic statin therapy in individuals older than 75 if well tolerated.[5] In this case, there is no evidence of a family history of premature heart disease and the LDL-C is below 160mg/dL. Data are not available for his coronary artery calcium level or ankle-brachial index, but his high sensitivity C-reactive protein is above the risk cutoff, possibly supporting initiation of pharmacotherapy for primary prevention.

FIGURE 3:

Additional ASCVD Risk Assessment Factors [5]

- **History of premature ASCVD in a first-degree relative** (< 55 years in males, <65 years in females)
- **LDL-C ≥ 160 mg/dL**
- **Coronary artery calcium score ≥ 300 Agatston units or > 75th percentile for age, sex, and ethnicity**
- **High sensitivity C-reactive protein ≥ 2 mg/L**
- **Ankle brachial index < 0.90**

To further determine whether statin therapy is appropriate, risk factors associated with adverse statin outcomes should be evaluated. Patient characteristics connected with statin adverse effects are summarized in Figure 1 *(page 39)*. To facilitate this evaluation, baseline measurement of liver transaminase levels (specifically alanine transaminase or ALT) is recommended in all patients prior to statin initiation.[5] Baseline measurement of creatine kinase is only warranted in those at risk for statin related myopathy, such as a history of statin intolerance or concomitant use of drugs that interact with statins.[5] This patient's initial laboratory testing reveals normal renal and liver function. He does not report a history of muscle disorders or other conditions or medications that would indicate potential issues with statin safety.

Based upon this patient's 10-year ASCVD risk, elevated high sensitivity C-reactive protein, and what appears to be a low propensity for adverse statin effects, it is decided to initiate a moderate intensity statin. He starts atorvastatin 10mg once daily. It is also noted that counseling for other cardiovascular risks should occur at this time, including assessment of eating and physical activity habits to encourage weight loss with his obese body mass index.

The patient presents to clinic for follow-up after one month. He reports adherence to his daily dose of medication but complains of muscle discomfort that he describes as "weakness" in both legs since initiating the statin. He denies any other symptoms at this time. What is the best approach to his symptoms?

The ACC/AHA guidelines recommend against routine laboratory monitoring after statin initiation.[5] However, assessment of symptoms of myopathy such as muscle pain, tenderness, cramping, weakness and fatigue should be performed at follow-up visits. Measurement of creatine kinase in symptomatic patients is necessary to investigate potential causes. Measurement of liver transaminases should occur if a patient complains of symptoms associated with hepatotoxicity such as abdominal pain, loss of appetite, dark-colored urine or yellow skin/sclera. Routine measurement is no longer supported. An additional monitoring parameter especially pertinent in the older population is evidence of statin-associated memory impairment or confusion.[5]

The ACC/AHA guidelines recommend a structured approach for management of muscle-related statin symptoms.[5] First, the statin should be discontinued during the evaluation process. Other causes should be investigated and ruled out, including vitamin D deficiency, rheumatologic disorders, or hypothyroidism. Based upon this patient's complaints, a creatine kinase level should be ordered.

The statin may be reinitiated at the same or lower dose if the symptoms resolve during this time in order to re-challenge the symptoms. If they recur, the statin should be discontinued and a lower dose of a different statin may be initiated once the symptoms resolve again. Increased doses of this statin can be attempted if the lower doses are tolerated.[5] All planning should involve discussion of patient preferences and re-evaluation of individualized risks and benefits that can change over time, especially in the elderly.

The limited data guiding the use of statin therapy in older individuals identifies several gaps requiring further research. Enrollment of adequate cohorts of men and women over age 75 in clinical trials is necessary to document clinical outcomes for both primary and secondary prevention of cardiovascular disease. Evaluation of clinical outcomes from alternative regimens utilized in statin-intolerant individuals, such as lower doses or non-statin medications, will further facilitate safe and effective care in patients of all ages.

CONCLUSION

ASCVD risk should be evaluated in all adult patients as ASCVD is the leading cause of death in the United States. Statins are important for the primary and secondary prevention of ASCVD. The Mayo Clinic has a useful online tool for demonstrating the primary prevention benefits and risks of statins.[25] Further research is needed to evaluate the benefits of statins in younger and older patients and better determinates on selection of statin intensity in a patient with diabetes.

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