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Practical Implementation of the 2013 AHA/ACC Blood Cholesterol Guidelines

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Opinion statement

Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of death in the United States. Choosing the appropriate patients for whom to initiate statin therapy to reduce the risk of ASCVD is of paramount importance. The new AHA/ACC guidelines on the treatment of cholesterol emphasize a patient-centered approach that shifts away from arbitrary LDL-C goals and recommends targeting statin therapy in patient populations that show ASCVD risk-reduction benefit. In addition, the guidelines emphasize lifestyle modification and the importance of the clinician-patient relationship in discussing ASCVD risk and initiating statin therapy.

Keywords

Atherosclerotic cardiovascular disease; Statins; Cholesterol guidelines

Introduction

Cardiovascular disease (CVD) remains the leading cause of death in the United States, and despite continued improvements in cardiovascular care, CVD rates remain unacceptably high [1]. Modification of cardiovascular risk factors is the central strategy in efforts to reduce CVD events. Lipid modification therapy has played an important role in cardiovascular risk reduction, and the HMG-CoA reductase inhibitors (statins) are amongst the most effective preventive medications available. There is consistent and compelling scientific evidence that statins reduce the risk of cardiovascular events and improve survival in patients with atherosclerotic vascular disease (secondary prevention). There is also strong evidence that statins reduce CVD events and improve survival in higher-risk primary prevention patients [2•, 3•]. As with all medications, however, statins also carry a risk of potential harms. In patients at significant risk of CVD, the benefits greatly outweigh the

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Compliance with Ethics Guidelines

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harms, but in patients at lower risk, the harms may outweigh the benefits. It is imperative, therefore, that statin therapy is targeted to those patients most likely to benefit.

Synopsis of recommendations

The new cholesterol guidelines released at the end of 2013 [4••] focus on several key points. First, clinicians should *encourage lifestyle modification*. Diet and exercise should serve as the platform upon which all other treatments are built. Reducing cardiovascular risk in adults is a long-term prospect, and engaging our patients in the process of lifestyle modification is of paramount importance. Second, the guidelines emphasize the use of medications proved to lower the risk of atherosclerotic cardiovascular disease (ASCVD)—namely, HMG-CoA reductase inhibitors (statins). Third, given that there is no evidence in the numerous trials in the literature to support treating to an arbitrary “target”, clinicians should *deemphasize treatment to LDL goals*. Finally, clinicians should use the *appropriate intensity* of statin therapy in the *appropriate group of patients* who have been shown to benefit from treatment based on the best evidence to date.

Who are the appropriate patients?

The new guidelines highlight four key groups who have been shown in randomized controlled trials and meta-analyses to benefit from statin therapy for reducing ASCVD:

1. Patients with clinical ASCVD. This group comprises individuals with prior MI, ACS, stable or unstable angina, stroke, TIA of atherosclerotic origin, or peripheral arterial disease. These patients need strong risk factor modification and intense lipid lowering for secondary prevention.
2. Patients with LDL-C elevation >190 mg/dL. These are individuals with familial hyperlipidemia and who will have a lifetime of exposure to adverse atherosclerotic effects of high cholesterol.
3. Patients 40–75 years of age with diabetes and with LDL-C 70–189 mg/dL (without clinical ASCVD). These patients are at increased lifetime risk for ASCVD and suffer worse morbidity and mortality after an ASCVD event [4••].
4. Individuals without diabetes or clinical ASCVD, but with an estimated 10-year risk of ASCVD of >7.5 % based on the Pooled Cohort Risk Calculator (available at <http://my.americanheart.org/cvriskscalculator> or <http://www.cardiosource.org/science-and-quality/practice-guidelines-and-quality-standards/2013-prevention-guideline-tools.aspx>). The relative reduction in ASCVD events is similar across the range of LDL levels in the primary prevention group based on data from randomized controlled trials [5, 6].

Primary prevention “controversy”

While most clinicians would not argue with initiating statin therapy for secondary prevention in patients with clinical ASCVD, very high LDL-C, or diabetes, there has been more discussion and disagreement about risks and benefits in the group with 10-year risk of ASCVD of >7.5 % using the Pooled Cohort Risk Calculator. Some have argued that the

calculator overemphasizes age in the calculation of risk and may overestimate risk based on validation cohorts [7, 8]. A recent validation study using data from the REasons for Geographical And Racial Differences in Stroke (REGARDS) study showed that observed and predicted five-year risk of ASCVD were similar for the clinically relevant primary prevention population [9]. It has been suggested that other cohorts in whom the calculator may overestimate 10-year ASCVD risk may be healthier and already on statin medication, which led to the discrepancy in the predicted and actual events. Clearly, the risk calculator will need ongoing validation in both the REGARDS and other populations. Moreover, the emphasis for this primary prevention population should be on the clinician-patient discussion about risks and benefits of statin therapy, and the guideline recommendation is not intended as a replacement for nuanced clinical decision-making.

Despite the controversy, the general concept that statin therapy is beneficial for certain higher-risk patients without clinical ASCVD is borne out in the evidence [2•, 3•]. Large meta-analyses from the Cholesterol Treatment Trialists and Cochrane Review demonstrate that statins reduce all-cause mortality, stroke, coronary disease, and fatal and non-fatal cardiovascular disease [2•, 3•], and these enormous benefits are conferred with an acceptable risk of adverse events. Moreover, from a health system perspective, the cost-effectiveness of statin medications and the magnitude of benefit to the larger society via reduction of ASCVD is significant [10, 11].

Statin intensity

The new guidelines focus not only on the appropriate patient groups outlined above, but also the appropriate intensity of statin therapy. The use of high-intensity statin medications lowers LDL-C levels by more than 50 %. Their use is recommended in most individuals in the groups discussed above: those with clinical ASCVD, patients with LDL-C of ≥ 190 , high-risk patients with diabetes, and those with a 10-year ASCVD risk ≥ 7.5 % (Table 1). Moderate-intensity statin therapy lowers LDL-C by 30–50 %, and is recommended for lower-risk patients with diabetes and for those with a 10-year ASCVD risk ≥ 7.5 % and intolerance to higher-intensity therapy. Moderate-intensity statin therapy can also be used in other high-risk patients who are intolerant of high-intensity statins or who are older than 75 years of age (Table 1).

Clinician-patient discussion

The critical central role of discussing the benefits and risks of statin therapy with our patients cannot be overemphasized. Patients should understand their risk for future ASCVD, and clinicians must reinforce strategies to reduce risk. As noted earlier, lifestyle modification is at the core of reducing ASCVD, and involves counseling patients on avoidance of smoking, pursuing regular exercise, maintaining a healthy weight, and following a heart-healthy diet [12]. Ten-year projected ASCVD risk should be a launching point for an ongoing discussion; guidelines and calculators cannot replace the nuances of individual decision-making. But we would also caution that aversion to *any* statin use in the primary prevention population with elevated 10-year ASCVD risk is unwarranted, given the benefits and safety profile of statins based on current data [2•, 3•]. Before initiating

therapy, clinicians should ascertain patient treatment preferences, interactions with other medications, and individualized risks and benefits (Fig. 1).

Monitoring and follow-up

Once clinicians decide to initiate the appropriate intensity of statin for the patient who will benefit, a baseline fasting lipid panel should be obtained. To assess for therapeutic response and adherence, a follow-up lipid panel should be evaluated in 1–3 months (high-intensity statins should lower LDL-C by 50 %, and moderate-intensity statins should lower LDL-C by 30–50 %). If the adherence and response are adequate, clinicians can monitor patients every 3–12 months, as appropriate. If response and/or adherence are not adequate, clinicians need to reinforce lifestyle modifications and the importance of adhering to medical therapy, and may decide to increase the intensity of statin therapy if the patient was previously on a lower- or moderate-intensity statin. These patients can be followed up again in 1–3 months to assess response and to monitor for side effects.

Some patients do develop intolerable side effects to statin therapy. The guidelines advocate ascertaining whether there is a true link between the symptom and the statin medication, and searching for possible causes of statin intolerance (such as drug–drug interactions). Once a link is confirmed, the medication can be stopped until the symptoms resolve, and the same statin can then be reintroduced at a lower dose, or an alternative statin medication can be used (Fig. 1). The ultimate goal should be putting such patients on the maximum tolerated statin dose that has no side effects.

Conclusions

The new ACC/AHA guidelines on the treatment of cholesterol to reduce ASCVD risk are a major step forward, with an emphasis on counseling patients regarding lifestyle changes, targeting patients that benefit from statins, using the appropriate intensity of statin therapy, and avoiding arbitrary LDL-C goals. Moreover, the assessment of future ASCVD risk in our patients and engaging them in a conversation about risks and benefits of statin therapy is a central component of the recommendations. Atherosclerotic cardiovascular disease is the leading cause of death in the United States, and these guidelines advocate a patient-centered approach in treating cholesterol to reduce the risk of ASCVD.

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Fig. 1.
Practical implementation of the ACC/AHA Cholesterol Guidelines.

Table 1**Appropriate Patients and Appropriate Statin Intensity***

Statin Intensity	Appropriate Medications	Appropriate Risk Groups
High-intensity statins: Lowers LDL-C by 50 %	Atorvastatin 40–80 mg Rosuvastatin 20–40 mg	<ul style="list-style-type: none"> • Patients with clinical ASCVD (prior stroke, MI, ACS, angina, PAD) • Patients with LDL-C ≥ 190 mg/dL • Patients 40–75 years of age with diabetes and LDL-C 70–189 mg/dL and 10-year ASCVD risk ≥ 7.5 % • Consider for primary prevention in patients with 10-year ASCVD risk ≥ 7.5 %
Moderate-intensity statins: Lowers LDL-C by 30–50 %	Atorvastatin 10–20 mg Rosuvastatin 5–10 mg Simvastatin 20–40 mg Pravastatin 40–80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg bid Pitavastatin 2–4 mg	<ul style="list-style-type: none"> • Patients with 10-year ASCVD risk ≥ 7.5 % if unable to tolerate high-intensity therapy • Patients 40–75 years of age with diabetes and LDL-C 70–189 mg/dL and 10-year ASCVD risk < 7.5 % • Consider for primary prevention in patients with 10-year ASCVD risk of 5–7.5 %** <p>Patients intolerant of high-intensity statins</p>

* Table adapted and modified from 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Cardiovascular Risk in Adults

** In these patients, clinicians should consider other factors that may modify risk for ASCVD, such as family history of early ASCVD (<55 years of age in first-degree male relative or <65 years of age in first-degree female relative), high-sensitivity CRP ≥ 2 mg/L, LDL-C ≥ 160 mg/dL, CAC score of ≥ 300 Agatston units or ≥ 75th percentile for age, sex and ethnicity, and ABI < 0.9.