AHA/ACC/Multisociety Cholesterol Guidelines: highlights

Ishwarlal Jialal and Sridevi Devaraj

Ther Adv Cardiovasc Dis

2019, Vol. 13: 1–3

DOI: 10.1177/1753944719881579

© The Author(s), 2019.
Article reuse guidelines: sagepub.com/journals-permissions

Correspondence to:
Ishwarlal Jialal
Veterans Affairs Medical Center, Mather, CA and Assistant Dean of Research, California North-State University, College of Medicine, 7300 Taron Road, Elk Grove, CA 95757, USA
kjialal@gmail.com

Sridevi Devaraj
Texas Children's Hospital and Baylor College of Medicine, Houston, TX, USA

Recently the American Heart Association/American College of Cardiology (AHA/ACC), in partnership with multiple societies, published their new guidelines for the management of blood cholesterol.[1] This is a very comprehensive guideline that embraces many clinical disorders, especially in primary prevention. At the outset, they provide the top 10 take-home messages.

In this commentary, we will focus largely on the highlights with respect to both primary and secondary prevention. These guidelines accept both fasting and nonfasting lipid panels for initial screening.

For both primary and secondary prevention, a heart-healthy lifestyle is emphasized in addition to drug therapies.[1] The guidelines emphasize that all adults should consume a healthy diet that includes vegetables, fruits, nuts, whole grains, lean vegetable or animal protein and fish, and minimize the intake of trans fats, processed meats, red meat, refined carbohydrates, and sweetened beverages. Calorie intake should be adjusted to avoid weight gain and promote weight loss. In addition, aerobic activity should be encouraged in adults. This should include three to four sessions of around 40 min duration of moderate-to-vigorous intensity physical activity per week.[1] Smoking cessation is strongly advised for all adults.

Statin therapy is recommended as the first-line drug treatment for primary prevention of atherosclerotic cardiovascular disease (ASCVD).[1] For patients with diabetes and familial hypercholesterolemia (FH) with low density lipoprotein-cholesterol (LDL-C) >190 mg/dl, there is no need for risk assessment prior to initiating statin therapy with moderate intensity statin therapy for the former initially. The guidelines emphasize the importance of assessment of ASCVD risk in primary prevention, and starting from age 20 years in order to initiate recommendations that optimize lifestyle and possible statin therapy. It is important to emphasize that the guidelines recommend a three-step approach to risk assessment in primary prevention for those 40–75 years: pooled cohort equation (PCE), use of risk enhancing factors to personalize the clinician-patient risk discussion and finally obtaining a coronary artery calcium (CAC) score if risk decision is still uncertain.[1] In asymptomatic adults aged 40–75 years, they suggest estimating 10-year ASCVD risk using race, diabetes, and sex-specific pooled cohort equation (PCE), which is the most robust measure to date. A PCE score <5% is low risk, 5–7.4% is defined as borderline risk, 7.5–19.9% as intermediate risk, and ⩾20% as high risk.[1] For high risk, one can initiate high-intensity statin therapy. For both borderline and intermediate risk categories, moderate intensity statin therapy can be initiated to achieve a LDL-C reduction between 30 and 49%. For low risk, lifestyle changes outlined above suffices.

In addition, for initiating or intensifying statin therapy, the guidelines suggest inclusion of risk enhancers: family history of premature ASCVD, persistent elevation of LDL-C ⩾160 mg/dl and non-HDL-cholesterol >190 mg/dl, chronic kidney disease, metabolic syndrome, conditions specific to women (pre-eclampsia and premature menopause), chronic inflammatory conditions such as rheumatoid arthritis, psoriasis, HIV, South Asian ancestry (the latter is a new addition to any of the previous guidelines).[1] Other risk-enhancing factors that were added include a persistently elevated triglycerides (TG) of ⩾175 mg/dl (measured on three occasions), which departs from the previous guidelines of TG > 150 mg/dl and could lead to misclassification of Metabolic Syndrome.[2] In addition, if measured, a lipoprotein (a) level ⩾50 mg/dl in patients with a family history of premature ASCVD is considered a risk-enhancing factor, a hsCRP >2 mg/l (which was previously classified as intermediate risk for

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (http://www.creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).

ASCVD) is a risk-enhancing factor, and the latter can guide therapy in selected individuals. Furthermore, in patients with TG ⩾200 mg/dl, an elevated apoB level of ⩾130 mg/dl (which equates to LDL-cholesterol of ⩾160 mg/dl) is considered a risk-enhancing factor.[1] In addition, an ankle-brachial index <0.9 is also a risk enhancer. If there is still uncertainty with respect to introducing statin therapy, assessment of CAC can be offered in patients at intermediate risk to guide statin therapy. If the CAC score is 0 Agatston units, in the absence of other major risk factors such as diabetes, family history of premature ASCVD and smoking it is reasonable to withhold therapy and reassess risk in 5–10 years.[1] If the CAC score is 1–99 units in persons over 55 years, it is reasonable to initiate statin therapy. If a patient has a CAC score ⩾100 units or ⩾75th percentile, it is prudent to initiate statin therapy.

Guidelines for statin therapy include patient's with ages between 20 and 75 years with LDL >190 mg/dl in whom high intensity statins should be initiated.[1] Also, all Type 2 diabetics, who are 40–75 years are recommended for moderate intensity statins, unless they have other risk-enhancing factors or PCE risk >20%, at which point high intensity statins should be considered for a >50% reduction in LDL-C.[1] These diabetes-specific risk enhancing factors include: long duration [⩾10 years for type 2 diabetes mellitus (T2DM) and ⩾20 years for type 1 diabetes mellitus (T1DM)], albuminuria (>30 µg/mg creatinine), estimated glomerular filtration rate (GFR) <60 ml/min/m^2, retinopathy, neuropathy, and an ABI < 0.9.[1] The guidelines recommend to intensify statin therapy in T2DM >50 years. However, there is limited evidence from clinical trials to support statin therapy in patients between 20 and 39 years, especially T1DM. Also in T2DM with ASCVD or 10 year risk >20%, the evidence base supports addition of ezetimibe to attain >50% reduction of LDL-C if the LDL threshold level >70 mg/dl.[1] Furthermore, proprotein convertase subtilism/kexin type9 (PCSK9) inhibitor therapy can be used if the LDL-C threshold exceeds 70 mg/dl and ASCVD is present.[3,4]

The guidelines suggest assessment of adherence and percentage response to LDL-C–lowering medications and lifestyle changes with repeat lipid measurement at 4–12 weeks after statin initiation or dose adjustment and repeated every 3–12 months as needed.[1]

Recommendations for children and adolescents were emphasized in the guidelines.[1] In this group, in all children and adolescents with lipid disorders related to obesity, the recommendation was made to intensify lifestyle therapy including caloric restriction and aerobic physical activity. Also, in this group, if there was a persistently elevated LDL >190 mg/dL or >160 mg/dL for a presentation consistent with FH, initiation of statin therapy was recommended without risk assessment. In patients with FH, the desirable LDL-C threshold should be <100 mg/dl, and ezetimibe can be added to maximum tolerated statin therapy if this threshold is exceeded.[1] Also, consideration can be given to use PCSK9 inhibitor therapy to mitigate ASCVD risk in FH if the threshold is still exceeded.[1] In children and adolescents with family history of early ASCVD or significant hypercholesterolemia, obesity, etc., measurement of nonfasting or fasting lipid profile is recommended as early as 2 years of age. The guidelines support the use of statins in children and adolescents >10 years who have FH and have not responded to 3–6 months of lifestyle changes; the intensity of treatment with statins should be based on severity of hypercholesterolemia.[1]

For the elderly, >75 years of age, evidence for statin therapy is not as strong, so clinical assessment of risk status in a clinician–patient risk discussion session is needed for deciding whether to initiate statin therapy considering comorbidities and longevity.[1] However, in a patient already on statin therapy, it is reasonable to continue therapy.

In secondary prevention of ASCVD, two treatment strategies for patients with and without very high risk are offered.[1] Very high risk is defined as a history of multiple major ASCVD events or one major ASCVD event with multiple high-risk conditions. The diagnosis of major ASCVD events included: recent acute coronary syndrome within 12 months, history of myocardial infarction, history of ischemic stroke, transient ischemic attacks, and symptomatic peripheral arterial disease (Ankle branchial index <0.9 with claudication or previous revascularizations or amputation) or aortic aneurysm.[1] High risk conditions included age ⩾65 years, heterozygous familial hypercholesterolemia, history of prior coronary artery bypass surgery or PCI outside of major ASCVD events (defined above), diabetes mellitus, hypertension, chronic kidney disease (estimated GFR <60 ml/min/m^2), current smoking,

persistent elevated low-density lipoprotein cholesterol (LDL-C) ⩾100 mg/dl despite maximum tolerated statin and ezetimibe, and history of congestive heart failure.[1] For patients with very high risk ASCVD, high intensity or maximum tolerated statin is the cornerstone of therapy. If the LDL-C threshold is ⩾70 mg/dl, ezetimibe should be added and if the patient still has a LDL-C threshold ⩾70 mg/dl or non-HDL-C ⩾100 mg/dl, adding a PCSK9 inhibitor is reasonable.[1,3]

In patients >75 years with ASCVD not at very high risk, the guidelines suggest to continue high intensity statin (achieve LDL-C reduction ⩾50%) or initiate moderate intensity therapy (achieve LDL-C reduction of 30–49%).[1] In patients ⩽75 years, high intensity statin therapy should be initiated. In these patients, if high intensity statin does not achieve a LDL-C < 70mg/dl or cannot be tolerated, the consideration of adding ezetimibe to a moderate- or high-intensity statin should be made.[1] In patients with heart failure due to ASCVD with reduced ejection fraction, with a reasonable like expectancy of 3–5 years, moderate-intensity statin could be considered, although, based on the primary end points of the studies to date, the data is far from convincing.[1] So the guidelines do not recommend PCSK9 inhibitor therapy for all patients with ASCVD, but only for those with very high-risk ASCVD. This is probably based on the major costs and long-term safety concerns of this exciting and potent class of drugs. Costs appear to have been reduced substantially since this guideline was published.

In conclusion, the guidelines are generally based on solid evidence. However, as pointed out above, the recommendation for statin therapy in diabetics <40 years is based on limited evidence. Also, it is unclear why PCSK9 inhibitor therapy is not indicated in all patients with ASCVD who have a LDL-cholesterol threshold >70 mg/dl, despite maximum tolerated statin and ezetimibe therapy. Finally the authors should be applauded for emphasizing a major stakeholder, the patient, in shared decision making.

Funding

The author(s) received no financial support for the research, authorship, and publication of this article.

Conflict of interest statement

The authors declare that there is no conflict of interest.

ORCID iD

Ishwarlal Jialal https://orcid.org/0000-0001-9113-2604

References

1. Grundy SM, Stone NJ, Bailey AL, *et al.* 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: executive summary: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *J Am Coll Cardiol* 2019; 73: 3168–3209.
2. Jialal I and Devaraj S. Potential implications of redefining the hypertriglyceridemia of metabolic syndrome. *Horm Mol Biol Clin Investig.* Epub ahead of print 20 June 2019. DOI: 10.1515/hmbci-2019-0014.
3. Sabatine M, Giugliano RP, Keech AC, *et al.* Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Eng J Med* 2017; 376: 1713–1722.
4. Jialal I and Singh G. Management of diabetic dyslipidemia: an update. *World J Diabetes* 2019; 10: 280–290.

Visit SAGE journals online
http://tac.sagepub.com
SAGE journals