Reexamining Recommendations for Treatment of Hypercholesterolemia in Older Adults

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The 2018 American College of Cardiology (ACC)/American Heart Association (AHA) guideline on the management of blood cholesterol recommends that “In adults 75 years of age or older with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), initiating a moderate-intensity statin may be reasonable.”1 If this recommendation was interpreted to mean that all patients meeting these criteria should receive statin therapy, an estimated 18 million older adults2 could potentially be at risk for adverse effects related to statins, based on limited evidence of a benefit of statin treatment in this age group. According to the introduction to the primary prevention section of the guideline, “For patients >75 years of age, RCT evidence for statin therapy is not strong.” The guideline also cautions about using age as a dominant risk factor, stating, “One limitation on the pooled cohort equation when applied to individuals is that age counts as a risk factor and dominates risk scoring with advancing age. Age is a powerful population risk factor but does not necessarily reflect individual risk.”

Summary recommendations in national guidelines should be consistent with the analysis of the supporting evidence. The recommendations should be derived without bias and written with minimal ambiguity.3 The tables in the ACC/AHA guideline show limited evidence supporting primary prevention in adults older than 75 years, and no evidence supporting a low-density lipoprotein (LDL) cholesterol cutoff greater than 70 mg/dL as a treatment threshold in this group.1 The selection of treatment and age thresholds is critical, because those factors determine the percentage of the population for which treatment is recommended.

In 8 primary prevention trials that involved individuals without diabetes, the average entry LDL cholesterol level was 140 mg/dL or higher,1,4 not 70 mg/dL or higher. The only primary prevention study with substantially lower entry LDL cholesterol level was the JUPITER trial, in which trial eligibility criteria included having an elevated highly sensitive C-reactive protein level (a separate risk factor for vascular disease). In the JUPITER trial, the study participants were a mean age of 66 years and had a mean entry LDL cholesterol level of 108 mg/dL, thereby representing a group with a younger age and higher LDL cholesterol level than addressed in the ACC/AHA recommendation.

When considering broad policy recommendations, it is important to recognize that the proportional benefit of managing high cholesterol is greater for adults younger than 65 years than for adults older than 65 years. Evidence of benefit for adults older than 65 years does not mean that the same is true for adults older than 75 years, and clinical trial data demonstrating benefits of statins for primary prevention are not available for adults older than 75 years.4

In the PROSPER trial, the only trial of statin treatment for patients with a mean age older than 75 years (N = 5804; mean age at study entry, 75.4 years), the mean entry LDL cholesterol level was 147 mg/dL, which is twice as high as the LDL cholesterol threshold for which statins are recommended in the ACC/AHA guidelines. In this trial, 2565 participants (44%) had established vascular disease, testing secondary prevention. In the primary prevention cohort of patients without vascular disease, there was no significant benefit of statins on the composite end point of coronary death, nonfatal myocardial infarction, and fatal or nonfatal stroke.5

The evidence in the ACC/AHA guideline shows no mortality benefit of statin treatment for individuals older than 75 years, whereas other reports suggest evidence of harm, including the possibility of increased mortality, with statin use in this age group.6 Observational data suggest no benefit of statin treatment for primary prevention among patients older than 75 years without diabetes.7 A meta-analysis of 28 randomized clinical trials showed a significant benefit of statins in patients with hypercholesterolemia and established vascular disease in all age groups, including patients older than 75 years. For patients with no history of vascular disease (ie, use of statins for primary prevention), there was a significant trend toward smaller proportional risk reduction from statin use with increasing age, and no significant benefit among patients older than 70 years.8

The AHA/ACC guidelines do not address when to discontinue statin treatment in adults older than 75 years. As patients age, the likelihood that they will have multiple comorbidities that require many medications increases. It is incumbent upon clinicians to weigh the importance of each medication to maximize value and minimize adverse effects.9 Decisions about continuing medications should be periodically reexamined. The decisions should be informed by...
evidence of benefit vs harm, as well as patients’ values and preferences, and the decision should be determined through an approach that emphasizes shared decision making.

Decisions about when to discontinue preventive therapy with a statin may fall into several categories. The first category involves frail older patients, including patients with severe dementia or other illnesses that will likely limit a patient’s life expectancy. For these patients, there is little likelihood of cardiovascular benefit for primary or secondary prevention from statins, so clinicians may consider stopping these drugs. The second category involves use of statins for secondary prevention in patients with a history of cardiovascular disease or events. For secondary prevention, the window during which a benefit may be seen is approximately 2 to 3 years. As long as preventing recurrent atherosclerotic cardiovascular disease is consistent with the goals of the patient and their family, statins for secondary prevention should be continued.

A third category involves patients with diabetes who are older than 75 years. While no randomized trial data are available for this group, observational data support continuing statins for all individuals in this group, including patients older than 85 years of age. The fourth category involves statin use for primary prevention for healthy adults aged 75 years and older. Knowing that the evidence is limited, and the likelihood of benefit is affected by age and risk factors, engaging in shared decision making with appropriate communication about the uncertainty of the evidence is recommended for this group of patients.

Guideline recommendations rest on a combination of evidence and judgment. Not all clinicians read the details of the supporting documentation, but most try to responsibly follow the core recommendations. Thus, the way in which recommendations are worded can have an important influence on how they are interpreted and implemented by clinicians. The AHA guidelines state that “it may be reasonable” to initiate statin therapy in adults 75 years of age or older with an LDL cholesterol level of 70 mg/dL to 189 mg/dL. However, because virtually all adults older than 75 years have an LDL cholesterol level higher than 70 mg/dL, the guidelines could be interpreted by some clinicians to recommend statin therapy to all healthy adults older than 75 years. It may, of course, also be reasonable not to prescribe statins to this group, because potential adverse effects, including myopathy, cognitive dysfunction, possible increase in type 2 diabetes, polypharmacy, and the potential effects of labeling healthy individuals with a medical diagnosis, are all critical concerns for older adults.

In linguistics, words and phrases have both denotative and connotative meanings. Denotative meaning refers to the literal meaning of words and phrases. “It may be reasonable to” and “it may be reasonable not to” denote essentially the same thing. Connotative meaning, on the other hand, refers to the emotional implications and associations that words and phrases carry, influenced by the context in which the words occur.

In the context of a clinician reading a guideline about the management of high cholesterol, the phrase “it is reasonable to treat...” implies that treating older adults with LDL cholesterol level higher than 70 mg/dL may be the recommended course of action. However, it is incumbent on practicing physicians not to simply adhere to guidelines, but to critically assess and interpret them in the context of each patient’s care. Recommendations for the use of statins in adults aged 75 years or older should be optimally determined though shared decision making about risk and benefit, as well as preferences and values, so that the recommendation best fits the needs of each individual patient.