Cholesterol Management in Older Persons

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Most atherosclerotic cardiovascular disease consists of coronary heart disease and stroke, and most atherosclerotic cardiovascular disease occurs in older persons. Randomized clinical trials with cholesterol-lowering drugs, notably statins, show reduced atherosclerotic cardiovascular disease events.[1,2] Statins are indicated when atherosclerotic cardiovascular disease is present. They further reduce risk in primary prevention, including older persons.[1,2] But their indications in primary prevention are less well defined than for secondary prevention. One view holds that virtually all older persons should be treated with statins.[2] Alternatively, a more targeted approach could be taken.[1] This viewpoint will compare both options for the older population.

Recent guidelines published by the American College of Cardiology (ACC) and the American Heart Association (AHA) expand statin use in primary prevention.[2] This expansion occurs largely in older persons. The guidelines recommend statins when 10-year risk for atherosclerotic cardiovascular disease is ≥7.5%. This makes most men over age 60 years and most women over age 70 years statin eligible. The ACC/AHA[2] claims that statin randomized clinical trials justify the 7.5% threshold; and because the majority of atherosclerotic cardiovascular disease events occur after age 70 years, the greatest public health benefit will occur in the older population.

It may be true that average population risk in older persons is ≥7.5%. For the whole population, chronological age correlates with risk. In some, but not all, people, atherosclerosis accumulates with age and raises risk. But, atherosclerosis burden in older individuals varies greatly. If we could distinguish between those with significant atherosclerotic burden and those with little or none, statin therapy could be employed more rationally.

Coronary artery calcium is the best available method for estimating atherosclerosis burden. Much insight can be gleaned from coronary artery calcium studies. ACC/AHA[2] notes that a coronary artery calcium score of ≥300

Agatston units is a reasonable threshold for statin treatment. The Multi-Ethnic Study of Atherosclerosis (MESA) and other studies reveal the predictive power of coronary artery calcium. In MESA, a 0 coronary artery calcium score confers a 10-year risk for coronary heart disease of only about 1.3%; and a score of 1-10 gives a 5.3% risk.[3] Importantly, most events accompanying low coronary artery calcium occur in smokers or patients with diabetes. MESA subjects with coronary artery calcium 1-100 have <7% risk for hard coronary heart disease regardless of the number of risk factors.[4] When coronary artery calcium score is 101-300, risk is relatively low, except when multiple risk factors were present. When coronary artery calcium is >300, risk is higher. Other studies give very similar results. They make 3 important points. First, a coronary artery calcium score <100 carries a low 10-year risk; consequently, statin therapy is unnecessary. Second, coronary artery calcium scores of 100-300 impart a borderline risk and make statins an option, particularly when multiple risk factors are present.[4] And third, statin therapy is reasonable when coronary artery calcium scores are >300, as noted by ACC/AHA guidelines.[2] In contrast with ACC/AHA recommendations,[2] coronary artery calcium studies demonstrate that not all older persons need statins.

According to a large coronary artery calcium study,[5] somewhat over half of men ages >65 years have coronary artery calcium scores >300. They clearly are candidates for statins.[2] Another quarter or so are borderline, making statins an option. But another quarter has low coronary artery calcium; here there is no need for cholesterol-lowering drugs. The situation is very different for older women.[5] Only a quarter have borderline coronary artery calcium, where statins are optional at most. The rest have low coronary artery calcium. Few have high coronary artery calcium (>300 Agatston units). This picture differs markedly from that painted by ACC/AHA guidelines,[2] where almost all older women are recommended for statin therapy. Admittedly, it is unrealistic to expect routine use of coronary artery calcium measurement in older persons. Nonetheless, the available data reveal that a large portion of older people does not need statins. The data suggest a need for more targeted risk assessment in this population.

Recent ACC/AHA guidelines[6] attempted to improve risk assessment by creating a risk-based algorithm derived from several epidemiological studies. Unfortunately, the algorithm appears to overestimate risk in lower-risk

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populations.[7] This is especially so where age alone and no other risk factors will trigger statin therapy in older persons. Therefore, other ways to assess risk can be considered. For example, treatment decisions could be based on the presence or absence of major risk factors (eg, cigarette smoking, diabetes, hypertension, and hypercholesterolemia). This would avoid statin use in older persons in the absence of major risk factors.

Statin therapy may be justified in older individuals with one or more major risk factors in addition to age. Consideration can be given to each of these risk factors. People who smoke cigarettes into older age are at higher risk for atherosclerotic cardiovascular disease events, both because they usually have smoked longer and they tend to be heavier smokers. In them, statin therapy is reasonable. Further, most investigators support use of statins in patients with type 2 diabetes.[1,2] These patients typically have multiple risk factors (eg, the metabolic syndrome). In fact, metabolic syndrome in the absence of type 2 diabetes doubles risk for atherosclerotic cardiovascular disease[8]; older individuals with diabetes or metabolic syndrome are good candidates for statins. Whether to use statins in persons with isolated hypertension is a matter for clinical judgment; if individuals are well controlled with antihypertensive agents, risk for stroke will be substantially reduced. If hypertension cannot be well controlled, statin therapy seems reasonable. Finally, an elevated serum cholesterol level (eg, low-density lipoprotein cholesterol >160 mg/dL) is commonly associated with more atherosclerosis, and probably justifies statin treatment. Recently, Ridker and Wilson[9] pointed out the advantages of a risk-factor-based approach to statin therapy rather than the so-called total-risk-based strategy.[6] The risk-factor-based approach seems especially apropos for the older population, in which age alone confers statin eligibility by the ACC/AHA algorithm.[2,6]

For some investigators, the benefit of generic statins in the elderly population appears self-evident. The ACC/AHA guidelines[2] imply that statins are highly efficacious, innocuous, and inexpensive. But there is insufficient randomized clinical trial evidence to document net benefit (favorable balance of efficacy, safety, and cost-effectiveness) in older individuals without major risk factors. ACC/AHA[2] went well beyond solid randomized clinical trial evidence in development of recommendations in the older population. Before net benefit in older, lower-risk persons can be assumed, more extensive research is needed.

The recent cholesterol guidelines[2] raised the important question of whether cholesterol-lowering drugs should be used as a public health measure or whether focused intervention in primary prevention is preferable. New guidelines appear to take a major step in the direction of transforming clinical management of cholesterol into a population approach. They largely identify older persons as the target population for this approach. The guidelines propose a bold public health experiment. But it is not an evidence-based experiment justified by randomized clinical trials in older persons. There is a lack of strong evidence that statin treatment for all confers a greater net benefit than a targeted treatment strategy.

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