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Low-density lipoprotein cholesterol goal attainment in high-risk family medicine patients

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BACKGROUND: The Adult Treatment Panel III guideline recommends a low-density lipoprotein-cholesterol (LDL-C) goal of <100 mg/dl for patients with coronary heart disease or risk equivalence (ie, other forms of atherosclerotic vascular disease [peripheral vascular disease, abdominal aortic aneurysm, cerebrovascular disease], diabetes). An optional LDL-C goal of <70 mg/dl is recommended for patients considered "very high risk." This category is not well defined, and clinical interpretation of this category varies.

METHODS: To define this category and to determine eligibility for an LDL-C goal of <70 mg/dl, 5 definitions of "very high risk" were developed. Patients with coronary heart disease or risk equivalence within the University of Colorado Family Medicine system over the course of 2 years were identified using International Classification of Diseases, 9th Revision codes (n = 445). Their medical records were evaluated retrospectively. Patients characterized as "very high risk" according to the 5 definitions were assessed for LDL-C <70 mg/dl goal attainment.

RESULTS: Twenty-seven patients did not have LDL-C measurements and were excluded. Using the 5 definitions, we discovered that prevalence as "very high risk" was 10.8% (atherosclerotic vascular disease [AVD] plus smoking), 19.1% (AVD plus diabetes), 21.5% (AVD plus metabolic syndrome plus uncontrolled hypertension or smoking), 47.1% (AVD plus metabolic syndrome), and 67.2% (All AVD), $P < .0001$. LDL-C <70 mg/dl was attained in 26.7%, 46.3%, 31.1%, 39.1%, and 35.2%, respectively ($P = .13$).

CONCLUSION: Classifying patients as "very high risk" is highly variable depending on individual definitions, but this does not appear to alter the rates of attaining an LDL-C goal of <70 mg/dl. When the Adult Treatment Panel IV guidelines are developed and issued, simplicity and clarity will be important in assisting clinicians in defining patient risk and developing LDL-C goals.

The Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III [ATP III]) focuses on lowering low-density lipoprotein-cholesterol (LDL-C) as the primary target for the prevention of major cardiovascular events. ATP III recommends an LDL-C goal of <100 mg/dl for patients deemed at "high risk" for a coronary event. High-risk patients have either coronary heart disease (CHD) or CHD risk equivalence. This classification includes those with existing atherosclerotic vascular disease (AVD), including previous myocardial infarction, angina without myocardial infarction, peripheral vascular disease, abdominal aortic aneurysm, carotid artery disease, and those with diabetes mellitus or a Framingham 10-year risk of >20%.[1]

After the publication of ATP III, 5 randomized controlled clinical trials were published that provided new evidence and further insight into the management of patients with dyslipidemia, especially those considered high risk.[2-6] These new

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data resulted in publication of the NCEP report "Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines."[7] This update added an optional, more aggressive, LDL-C goal of <70 mg/dl for patients at "very high risk" for a coronary event. Data published subsequent to the NCEP update appear to support the optional, lower, LDL-C goal.[8-10]

In the NCEP update report, patients at "very high risk" are classified as having "established CVD plus 1) multiple major risk factors (especially diabetes), 2) severe and poorly controlled risk factors (especially continued cigarette smoking), 3) multiple risk factors of the metabolic syndrome (especially high triglycerides ≥200 mg/dl plus non-high-density lipoprotine cholesterol [HDL-C] ≥130 mg/dl with low HDL-C [< 40 mg/dl]), and 4) acute coronary syndrome."[7] This definition of "very high risk" may be considered vague by some clinicians and can leave substantial room for interpretation. In addition, the NCEP update report recommends that if a lipid-lowering regimen is initiated, it is prudent to initiate a drug and dose that will provide at least a 30-40% LDL-C reduction, regardless of the baseline LDL-C.[7]

The primary objectives of this study were to categorize patients with CHD or CHD risk equivalence as eligible for an LDL-C goal of <70 mg/dl according to 5 different definitions of "very high risk" and to assess LDL-C < 70 mg/dl goal attainment rates based on these definitions. Secondary objectives included describing the percentage of patients prescribed a lipid-lowering regimen capable of providing at least 30-40% LDL-C reduction, describing the percentage of patients achieving an LDL-C of <100 mg/dl and <70 mg/dl overall, and estimating which lipid-lowering medication changes would be required to achieve LDL-C goals of <70 mg/dl and <100 mg/dl in subjects not already achieving these values.

Methods

Five specific definitions of "very high risk" were created based on the definition provided in the NCEP report update.[7] The specific definitions were developed to simulate examples of what clinicians might use to characterize a patient as "very high risk." The definitions range from restrictive to more open interpretations. The 5 definitions were as follows: 1) presence of AVD, 2) AVD plus continued cigarette smoking, 3) AVD plus presence of the metabolic syndrome, 4) AVD plus the metabolic syndrome plus one additional major risk factor, and 5) AVD plus diabetes mellitus. The metabolic syndrome was considered present if patients had at least 3 of the 5 cardiometabolic criteria (increased blood pressure [≥ 130 mm Hg systolic or ≥85 mm Hg diastolic] or drug treatment for hypertension; elevated fasting glucose [≥ 100 mg/dl] or drug treatment for increased fasting glucose; reduced HDL-C [< 40 mg/dl for men, <50 mg/dl for women] or drug treatment for reduced HDL; increased triglycerides [≥ 150 mg/dl] or drug treatment for elevated triglycerides; and abdominal obesity).[11] Body mass index (≥30 kg/m^2) was used in place of increased waist circumference in defining abdominal obesity because waist circumference measures were not available in the medical record.[12]

Patients with AVD or diabetes mellitus were identified by the use of International Classification of Diseases, 9th Revision codes generated from University of Colorado Family Medicine Clinics (250.xx, 357.2, 410.xx, 411.0, 411.1, 411.81, 411.89, 412, 413.0, 413.1, 413.9, 414.xx, 429.xx, 434.00, 434.01, 435.8, 435.9, 436, 437.0, 437.1, 440.0, 440.8, 440.9, 441.4, 443.89, or 443.9). The patients identified were seen for a clinic visit between January 1, 2005, and December 31, 2006. Exclusion criteria included patients without an LDL-C value. Patients with a Framingham risk score of >20%, but without clinically evident CHD or CHD risk equivalence, were not included as "high risk" because the electronic medical record was unable to identify them.

For the secondary objective of estimating the modification of the LDL-C−lowering regimen needed to achieve LDL-C goal recommendations, an LDL-C−lowering algorithm was developed (Fig 1). On the basis of the algorithm, a doubling of statin dose was assumed to provide another 10 mg/dl reduction in LDL-C. For example, a patient currently receiving atorvastatin 10 mg daily with an LDL-C of 120 mg/dl would have a 10 mg/dl LDL-C lowering when given a dose increase to atorvastatin 20 mg daily. In addition, the use of a statin with greater potency could also result in a 10 mg/dl reduction in LDL-C.

Each step increase in the algorithm represents a 10 mg/dl decrease in LDL-C. This stepwise approach was adapted from a previously published therapeutic conversion algorithm and from available clinical evidence.[13,14] The addition of ezetimibe to the current regimen was also an option, and its effect on lowering LDL-C was determined from available clinical evidence. When added as monotherapy to patients currently receiving no cholesterol-lowering medication, ezetimibe has been shown to lower LDL-C by approximately 25-30 mg/dl.[15,16] When added to or co-administered with ongoing atorvastatin, simvastatin, pravastatin, fluvastatin, lovastatin, or rosuvastatin therapy, ezetimibe provides an additional 22-33 mg/dl decrease in LDL-C.[17-27] Therefore, we assumed that the addition of ezetimibe, either as monotherapy or as add-on therapy to the current cholesterol-lowering regimen, would provide an additional 25 mg/dl reduction in LDL-C, or a 2.5-step increase. The algorithm allowed us to predict the LDL-C−lowering regimen modification needed to attain the desired LDL-C goal.

The Allscripts electronic medical record (Allscripts, Chicago, IL) was used to retrospectively collect data. Data collected included age, sex, smoking status, diagnosis, HgbA1c, lipid panel results, fasting blood glucose, most recent blood pressure measurement, body mass index, and currently prescribed LDL-C lowering, HDL-C raising, triglyceride lowering, diabetes, or hypertension pharmacotherapy.

Statistical analysis

Descriptive statistics were used for all data and are presented in terms of mean (± standard deviation) and