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Attainment of low-density lipoprotein cholesterol goals in coronary artery disease

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BACKGROUND: The National Cholesterol Education Program Guidelines offer an optional low-density lipoprotein cholesterol (LDL-C) goal of less than 70 mg/dL for very high-risk patients with coronary artery disease (CAD). This study evaluated the extent to which this recommendation can be attained by the use of currently available lipid-lowering therapies.

METHODS: A retrospective, cross-sectional study of patients in the Kaiser Permanente Colorado healthcare system 18 years of age or older with CAD and a predetermined LDL-C goal less than 70 mg/dL. The LDL-C most proximal, but within 1 year before April 1, 2008, was deemed the qualifying LDL-C and used to determine LDL-C goal attainment. Lipid-lowering medication(s) for those attaining goal and factors associated with failure to attain LDL-C goal also were identified.

RESULTS: A total of 7427 patients were included in the study. A total of 3226 patients attained a LDL-C less than 70 mg/dL. The majority (92.4%) attaining goal were receiving statin monotherapy or in combination compared with 81.3% not at goal ($P < .001$). More than one-half attained goal on statin monotherapy with 70.7% at moderate- to high-potency doses and 87.4% on generically available statin. Nearly one-third attaining goal received statin in combination. Ezetimibe (70.6%) was most frequently used with statin. Factors independently associated with failure to attain a LDL-C less than 70 mg/dL were age younger than 65 years, patients not receiving statin, a history of creatine kinase elevation, and female sex.

CONCLUSION: This study reports the greatest rate of LDL-C less than 70 mg/dL goal attainment in a very high-risk population with CAD to date. However, despite a system dedicated to aggressively treat to a LDL-C goal of less than 70 mg/dL, success in the majority is a challenge with the currently available therapies.

Several large, randomized clinical trials have demonstrated the importance of aggressively lowering low-density-lipoprotein cholesterol (LDL-C), primarily through the use of 3-hydroxy-3-methylglutaryl-coenzyme A lyase (ie, HMG-CoA) reductase inhibitors (statins) in patients

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with established atherosclerotic coronary artery disease (CAD).[1–6] Traditionally, clinical practice guidelines have recommended a LDL-C goal of less than 100 mg/dL for patients with CAD[7]; however, a number of subsequent clinical trials[4,8–12] have suggested that lowering the LDL-C to well below 100 mg/dL is associated with further reductions in cardiovascular morbidity and mortality. Although these trials did not target a prespecified LDL-C goal, the results prompted revisions to the recommended clinical practice guidelines.[13] The revised guidelines recommend an optional LDL-C goal less than 70 mg/dL for patients with CAD at "very high-risk" for recurrent events. "Very high-risk" included patients with established CAD plus diabetes mellitus, peripheral arterial disease, symptomatic carotid disease, poorly controlled cardiovascular risk factors (eg, current smoker, uncontrolled hypertension), and multiple risk factors for metabolic syndrome or acute coronary syndrome.[13]

The attainability of the optional LDL-C treatment goal with the current armamentarium of lipid-lowering therapies (LLT) has been scrutinized.[14–16] The National Health and Nutrition Examination Survey reported that only 40.5% of patients with CAD attained a LDL-C less than 100 mg/dL,[17] a result that is consistent with numerous other reports.[18–26] Few data on the percentage of patients who actually attain a LDL-C less than 70 mg/dL in real-world clinical practice exist. The purpose of this study was to report: 1) the percentage of patients with CAD who attained a predetermined LDL-C goal of less than70 mg/dL; 2) to describe the LLT(s) that patients at goal were receiving; and 3) to identify factors independently associated with failure to attain the LDL-C goal.

Methods

Study design and setting

This retrospective, cross-sectional analysis of patients with CAD was conducted at Kaiser Permanente Colorado (KPCO). KPCO is an integrated health-care delivery system providing services to more than 460,000 members at 18 medical offices in the Denver-Boulder metropolitan area. KPCO uses an electronic medical record in which all office visit, vital, laboratory, and pharmacy data are housed. The majority of members receive prescription medications from KPCO pharmacies for a copayment.

Starting in 1998, nearly all KPCO members with CAD have been enrolled into a comprehensive cardiac risk reduction service called the Clinical Pharmacy Cardiac Risk Service (CPCRS). The CPCRS is a clinical pharmacy specialist-managed, physician-directed, protocol-driven secondary cardiovascular prevention service that uses a systems-based approach to focus on the long-term medication management of more than 13,000 patients with CAD.[27–29] Patients enrolled in CPCRS include those with a history of a previous myocardial infarction, coronary artery bypass graft surgery, or percutaneous coronary intervention. Clinical pharmacy specialists review all patients enrolled in CPCRS and establish a LDL-C treatment goal collaboratively with physicians. All patients receive ongoing counseling on therapeutic lifestyle modifications. Lipid-lowering and other heart protective therapies are initiated and titrated as indicated. Patients enrolled in CPCRS are managed under collaborative drug therapy management protocols, with each patient being offered all available evidence-based therapies in attempts to reach LDL-C treatment goals.

Patient population

All active KPCO members 18 years of age or older that were enrolled in CPCRS for at least 1 year before April 1, 2008, were eligible for the study. Of the 10,000 members eligible for inclusion, 2188 had a treatment goal other than less than 70 mg/dL and were excluded. An additional 385 members were excluded because a LDL-C value was unavailable. A total of 7427 patients were included in the study.

Data collection

Laboratory data were obtained by the use of integrated laboratory databases and included LDL-C, alanine aminotransferase (ALT), and creatine kinase (CK) values. The Friedewald formula was used to calculate LDL-C values in most instances. However, in cases of triglycerides greater than 400 mg/dL, a direct LDL-C measurement was used. The LDL-C measure most proximal to April 1, 2008, but within the previous 365 days, was deemed the qualifying LDL-C and was used to determine attainment of LDL-C goal. Additionally, the highest LDL-C value recorded during a patient's membership at KPCO was collected. A history of elevated ALT was defined as $\geq$3 times the upper limit of normal ($\geq 3\times$ ULN). Patients with a previous CK value between $\geq 3\times$ ULN and $<10\times$ ULN, a CK $>10\times$ ULN, or with a history of rhabdomyolysis (identified through International Classification of Diseases, 9th Revision codes) were also identified.

Administrative and validated disease-management databases within KPCO were used to collect demographic, CAD risk factor (smoking status, diabetes mellitus, peripheral artery disease, and chronic kidney disease), CAD event history, and LDL-C treatment goal data. Additional comorbidity and CAD risk factor data were identified by the use of International Classification of Diseases, 9th Revision, diagnosis codes from the electronic medical record within 180 days of the date of the qualifying LDL-C value. Chronic kidney disease was defined as a glomerular filtration rate (GFR) less than 60 mL/min and was calculated by use of the abbreviated modification of diet in renal disease formula. Additionally, patients with a GFR less than 30 ml/min were identified. A chronic disease score (CDS), which