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Original Articles

Achieving optimal lipid values in patients with dyslipidemia is associated with reduced risk of cardiovascular events

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BACKGROUND: Cardiovascular (CV) event risk is significantly lower in patients with combined low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) at desired levels versus those without lower levels. However, this has not been investigated relative to specific patterns of baseline lipid abnormalities.

OBJECTIVE: To evaluate the association between desired combined lipid value achievement and risk of CV events in patients with different baseline lipid profiles.

METHODS: A retrospective managed care database analysis among treatment-naïve adults with elevated CV event risk, ≥12 months follow-up, and full lipid panel from January 1, 2001 to December 31, 2001 plus ≥1 panel before a CV event or study end. Patients were stratified into three baseline cohorts: isolated high LDL-C (Cohort 1), high LDL-C + low HDL-C or high TG (Cohort 2), and high LDL-C, low HDL-C, and high TG (Cohort 3). CV event risk stratified by combined desired lipid value achievement was assessed in each cohort.

RESULTS: Achievement of combined desired lipid values/median days to achievement was 29% in 385 days (Cohort 1), 11% in 413 days (Cohort 2), and 7% in 505 days (Cohort 3). Achievement of combined desired lipid values was associated with an adjusted 25%–46% lower CV event risk in Cohort 1 (hazards ratio, 0.75; 95% confidence interval 0.65–0.87), Cohort 2 (hazards ratio, 0.54; 95% confidence interval 0.43–0.67), and Cohort 3 (hazard ratio, 0.54; 95% confidence interval 0.37–0.78).

CONCLUSION: Patients with combined desired lipid values had lower risk of CV events versus those without such values. The risk reduction was greatest among patients with multiple lipid abnormalities, suggesting a potential benefit of interventions targeting low HDL-C and/or high TG in addition to high LDL-C.

Cardiovascular (CV) disease affects more than 80 million adult Americans and accounts for one of every 2.8 deaths.[1] Elevated levels of low-density lipoprotein cholesterol (LDL-C), high triglycerides (TG), and low high-density lipoprotein cholesterol (HDL-C) values are major inde-

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pendent risk factors for CV disease morbidity and mortality that are frequently encountered in the clinical setting.[1,2] Evidence-based guidelines for the modification of lipid risk factors provide definitions for therapeutic goal values for LDL-C and suggest targets for HDL-C and TG in different subgroups of patients.[3–5] These guidelines primarily focus on lowering of LDL-C using statins. More recent guidelines suggest even more aggressive LDL-C desirable levels in very high-risk patients.[3–6] However, although aggressive LDL-C lowering is an important component of current approaches to CV risk reduction, recent evidence suggests that this strategy yields small and incremental benefit in terms of reduction in CV events. As such, there is increasing focus on the need to additionally increase HDL-C or lower TG as potential targets of therapy.[7–12] Although definitive studies have not been completed regarding further risk reduction by using these as secondary targets, current evidence-based guidelines suggest use of niacin or fibrate therapy when HDL-C is low or non–HDL-C is elevated in high-risk individuals.[3–5]

Previous research in diverse populations with elevated CV risk has demonstrated that multiple lipid abnormalities, characterized by combinations of undesired or nonoptimal values for LDL-C, HDL-C, non–HDL-C, and TG, are frequent. Further, simultaneous or combined achievement of desired or optimal levels for these lipid fractions is uncommon in routine clinical practice[13–16] in the United States. This observed high prevalence of multiple lipid abnormalities and low rates of combined lipid value achievement within desirable levels appears in part to be related to underutilization of guideline-recommended pharmacotherapy, in particular therapy targeted to HDL-C and TG abnormalities.[13–16] The potential for this is noteworthy, as the population-based risk of CV events over time appears to be significantly lower in patients who have desired levels of LDL-C, HDL-C, and TG compared to patients who do not.[17]

Although this prior research provides important information about the relationship between desirable lipid values and CV outcomes on a broad population basis, it does not provide detail into the same on the basis of the pattern of dyslipidemia at initial presentation. The primary purpose of the present investigation is to determine the association between achievement of desired, or optimal, combined lipid values and risk of CV events in groups of untreated patients with distinct patterns of abnormalities in LDL-C, HDL-C, and TG values at baseline.

Methods

Study design

The study was a longitudinal retrospective cohort analysis based on healthcare claims from a large southeastern United States managed care organization. The organization's administrative medical and pharmacy claims records provided individual patient data on demographics, clinical diagnosis, serial plasma lipid levels, prescription drug treatment, and incident clinical events due to CV disease over five and a half years.

Data source

This longitudinal retrospective cohort analysis was conducted within the HealthCore Integrated Research Database (HIRD) using administrative claims and laboratory data from January 1, 1999 to June 30, 2004 from 2.1 million Medicare and non-Medicare eligible members. The fully integrated dataset included date-stamped, linked medical, pharmacy, and laboratory encounters complete with laboratory results and eligibility files. Patient identity was masked throughout in a limited data set format, in accordance with the Health Insurance Portability and Accountability Act (HIPAA) of 1996.

Patient selection

The patient selection scheme is shown in Figure 1. Adult patients (≥18 years of age) with results from at least one full lipid panel present in a 2-year study intake period between January 1, 2000 and December 31, 2001 were included. A full lipid panel was defined as the presence of LDL-C, HDL-C, TG, and total cholesterol results for a patient on the same calendar day, with that date serving as the baseline laboratory date. Patients were required to have a minimum continuous data stream of 12 months pre- and post-baseline laboratory data. To ensure that patients were naïve to lipid pharmacotherapy at baseline, only those without a National Drug Code (NDC) for lipid-altering therapy in the 6-month period prior to the baseline laboratory date were included for the study.

Patient risk stratification

Patients with definable CV risk assessed at the time period preceding and including the baseline lipid panel date were included in the analysis, and were categorized into two risk groups: elevated risk primary prevention (ERPP) or CHD/CHD Risk Equivalent (CHD/CHD-RE) (Table 1). Categorization was based on age, gender, baseline lipid values, previous and concurrent diagnoses and procedures, and medication usage. Patients whose risk status could not be clearly identified as ERPP or CHD/CHD-RE were not included for analysis. Achievement of optimal lipid values (Table 2) was determined by risk level as per evidence-based guidelines for LDL-C and suggested acceptable thresholds for HDL-C and triglycerides.[2–5]

Study cohort definition and selection

The remaining sample was stratified into three mutually exclusive cohorts by baseline lipid laboratory values compared to definitions of optimal values appropriate for each