

Lipid levels in patients hospitalized with coronary artery disease: An analysis of 136,905 hospitalizations in Get With The Guidelines

Amit Sachdeva, MD,^a Christopher P. Cannon, MD,^b Prakash C. Deedwania, MD,^c Kenneth A. LaBresh, MD,^d Sidney C. Smith, Jr, MD,^e David Dai, MS,^f Adrian Hernandez, MD,^f and Gregg C. Fonarow, MD^a on behalf of the GWTG Steering Committee and Hospitals Los Angeles and San Francisco, CA; Boston and Waltham, MA; and Chapel Hill and Durham, NC

Background Lipid levels among contemporary patients hospitalized with coronary artery disease (CAD) have not been well studied. This study aimed to analyze admission lipid levels in a broad contemporary population of patients hospitalized with CAD.

Methods The Get With The Guidelines database was analyzed for CAD hospitalizations from 2000 to 2006 with documented lipid levels in the first 24 hours of admission. Patients were divided into low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), and triglyceride categories. Factors associated with LDL and HDL levels were assessed along with temporal trends.

Results Of 231,986 hospitalizations from 541 hospitals, admission lipid levels were documented in 136,905 (59.0%). Mean lipid levels were LDL 104.9 ± 39.8 , HDL 39.7 ± 13.2 , and triglyceride 161 ± 128 mg/dL. Low-density lipoprotein cholesterol <70 mg/dL was observed in 17.6% and ideal levels (LDL <70 with HDL ≥ 60 mg/dL) in only 1.4%. High-density lipoprotein cholesterol was <40 mg/dL in 54.6% of patients. Before admission, only 28,944 (21.1%) patients were receiving lipid-lowering medications. Predictors for higher LDL included female gender, no diabetes, history of hyperlipidemia, no prior lipid-lowering medications, and presenting with acute coronary syndrome. Both LDL and HDL levels declined over time ($P < .0001$).

Conclusions In a large cohort of patients hospitalized with CAD, almost half have admission LDL levels <100 mg/dL. More than half the patients have admission HDL levels <40 mg/dL, whereas $<10\%$ have HDL ≥ 60 mg/dL. These findings may provide further support for recent guideline revisions with even lower LDL goals and for developing effective treatments to raise HDL. (Am Heart J 2009;157:1111-7.e2.)

Serum total cholesterol and low-density lipoprotein cholesterol (LDL) significantly contribute to atherosclerosis, and its clinical manifestations including acute coronary events. Numerous studies have demonstrated that lipid-lowering therapy reduces the risk of first or recurrent cardiovascular events and improves survival in patients with coronary artery disease (CAD).¹ The National Cholesterol Education Program (NCEP) Adult Treatment

Panel guidelines have set LDL level treatment goals based on categories of patient risk.² In more recent NCEP guideline updates, new categories of patients at high risk of coronary heart disease (CHD) events have been identified including those patients with existing CHD, other atherosclerotic vascular disease, or diabetes mellitus, and lower LDL treatment goals for such patients have been established to decrease their cardiovascular risk more effectively.

From the ^aDepartment of Medicine, UCLA Medical Center, Los Angeles, CA, ^bBrigham and Women's Hospital & Harvard Medical School, Boston, MA, ^cDepartment of Cardiology, VA Medical Center/UCSF School of Medicine, San Francisco, CA, ^dMasspro, Waltham, MA, ^eUniversity of North Carolina School of Medicine, Chapel Hill, NC, and ^fDuke Clinical Research Institute, Durham, NC.

The Get With The Guidelines Program is supported by the American Heart Association (Dallas, TX) in part through an unrestricted education grant from the Merck Schering Plough Partnership (North Wales, PA) who did not participate in the design, analysis, preparation, review, or approval of this article.

Financial disclosures: Amit Sachdeva, MD (none); Christopher P. Cannon, MD (grants: Accumetrics [San Diego, CA], AstraZeneca [Wilmington, DE], Bristol-Myers Squibb [New York, NY], GlaxoSmithKline [Philadelphia, PA], Merck [Whitehouse Station, NJ], Sanofi-Aventis [Bridgewater, NJ], Schering Plough [Kenilworth, NJ]); Prakash C. Deedwania, MD (consultant of AstraZeneca and Pfizer [New York, NY]); Kenneth A. LaBresh, MD (none);

Sidney C. Smith, Jr., MD (none); David Dai, PhD (employee of Duke Clinical Research Institute [Durham, NC]); Adrian Hernandez, MD (none); Gregg C. Fonarow, MD (research from Pfizer and GlaxoSmithKline; consultant and honorarium from Abbott, AstraZeneca, GlaxoSmithKline, Merck, Pfizer, and Schering Plough; and chair of the Get With the Guidelines Steering Committee).

Dr. Todd D. Miller served as guest editor for this manuscript.

Submitted May 9, 2008; accepted August 6, 2008.

Reprint requests: Gregg C. Fonarow, MD, Ahmanson-UCLA Cardiomyopathy Center, UCLA Medical Center, 10833 LeConte Avenue, Room 47-123 CHS, Los Angeles, CA 90095-1679.

E-mail: gfonarow@mednet.ucla.edu

0002-8703/\$ - see front matter

© 2009, Mosby, Inc. All rights reserved.

doi:10.1016/j.ahj.2008.08.010

A number of studies have suggested that total cholesterol and LDL levels have been decreasing in the general US population.³ Although lipid levels and temporal trends in the general population have been well studied, lipid levels among contemporary patients hospitalized with CAD have not. This study analyzed data from the American Heart Association's Get With The Guidelines (GWTG) CAD Program from 2000 to 2006. A broad cohort of patients hospitalized with CAD among participating hospitals in which lipid levels were obtained within the first 24 hours of admission were studied. The proportion of patients falling into each NCEP category for LDL, high-density lipoprotein cholesterol (HDL), and triglycerides were assessed, overall and for clinically relevant subgroups, as well as factors associated with admission lipid levels. Temporal trends during the period of the study were also analyzed.

Methods

Details of GWTG CAD have been previously published.⁴ In brief, the American Heart Association (Dallas, TX) launched the GWTG program to support and facilitate the improvement of the quality of care of patients with cardiovascular disease. Get With The Guidelines uses a Web-based patient management tool (Outcome Sciences Inc, Cambridge, MA) to collect clinical data, provide decision support, and provide real-time online reporting features. Data collected included patient demographics, medical history, symptoms on arrival, results of laboratory testing, in-hospital treatment and events, discharge treatment and counseling, and patient disposition. Outcome Sciences, Inc, serves as the data collection and coordination center for GWTG.

Patient population

This study includes patients enrolled from the 541 hospitals participating in GWTG-CAD program that includes teaching and nonteaching, rural and urban, and large and small hospitals from all census regions of the United States. The patient population included patients hospitalized with confirmed clinical diagnoses of CAD, including patients with acute coronary syndromes, stable CAD hospitalized for revascularization, and patients with documented CAD hospitalized for reasons other than heart failure. Case finding was based on clinical identification of patients with CAD diagnoses or Joint Commission *International Classification of Diseases, Ninth Revision* identification of CAD diagnoses with clinical verification for data abstraction.

Data were collected on patients hospitalized at participating hospitals between January 1, 2000, and April 30, 2006. The data elements collected had written definitions and were gathered using common specifications for all participants. Using the internet-based system, data quality was monitored, and reports were generated to assure the completeness and accuracy of the submitted data. All participating institutions were required to comply with local regulatory and privacy guidelines and to submit the GWTG protocol for review and approval by their institutional review board. Because data were used primarily at the local site for quality improvement, sites were granted a waiver of informed consent under the common rule. The Duke

Clinical Research Institute (Durham, NC) serves as the data analysis center and analyzed the aggregate deidentified data for research purposes.

Patient characteristics, quality of care, and in-hospital procedures data were collected and included demographics, past medical history, use of lipid-lowering medications as an outpatient before hospitalization, cardiac diagnosis of patients on presentation, vital signs, admission laboratories, cardiac procedures, and discharge quality of care measures. Lipid levels obtained within the first 24 hours of admission were as analyzed by the local hospital laboratory and as recorded in the medical record. The study population included patients with CAD in the database with lipid levels documented in the first 24 hours of admission. Patients with heart failure (n = 38,579) were excluded from the study.

Statistical analysis

Patients were divided into categories based on admission lipid levels: LDL <70, 70-100, 100-130, 130-160, and ≥ 160 mg/dL; HDL <40, 40-60, and ≥ 60 mg/dL; and triglyceride <150 and ≥ 150 mg/dL. Wilcoxon rank sum tests were used for continuous variables and χ^2 tests for categorical variables. The mean ($\pm$ SD) and percentages were reported for continuous and categorical variables, respectively. The Kruskal-Wallis test was used to compare temporal trends in lipid levels. Multivariable regression analysis using Generalized Estimation Equations (GEE) was performed to determine patient characteristics predictive of LDL and HDL levels. The GEE approach adjusts for patient demographics and baseline clinical status and considers the clustering effect within hospitals. Patient age, gender, race, body mass index, medical history (hypertension, dyslipidemia, diabetes, renal insufficiency, prior myocardial infarction [MI], smoking, heart failure, and stroke), admission diagnoses, and prior use of lipid-lowering medications were included initially in the multivariable model, and then factors for which $P \geq .05$ were removed from the logistic regression model. A P of <.05 was considered significant for each test. Multivariable analyses were also performed for variables predictive of LDL ≥ 100 mg/dL and HDL <40 mg/dL. All analyses were performed using SAS software (version 8.2, SAS Institute Inc, Cary, NC).

Results

During the 76 months of the study in 231,896 CAD hospitalizations from 541 hospitals, lipid levels were obtained in the first 24 hours of hospitalization in 136,905 (59.0%). Patients with and without lipid levels obtained on admission showed modest differences: age (65 vs 69 years), female sex (63% vs 59%), prior CHD, other atherosclerotic vascular disease, or diabetes (46% vs 40%), and treatment with lipid-lowering medications before hospitalization (21% vs 16%). The clinical characteristics of the patients with documented admission lipid levels are listed in Table I. The mean age of the population was 65 ± 14 , and 62.7% were male. The cohort were 65.2% white, 6.7% black, 5.7% Hispanic, and 2.3% Asian. Cardiovascular risk factors and comorbidities were frequently present with 54.2% having hypertension, 26.2% having diabetes, and 30.4% being

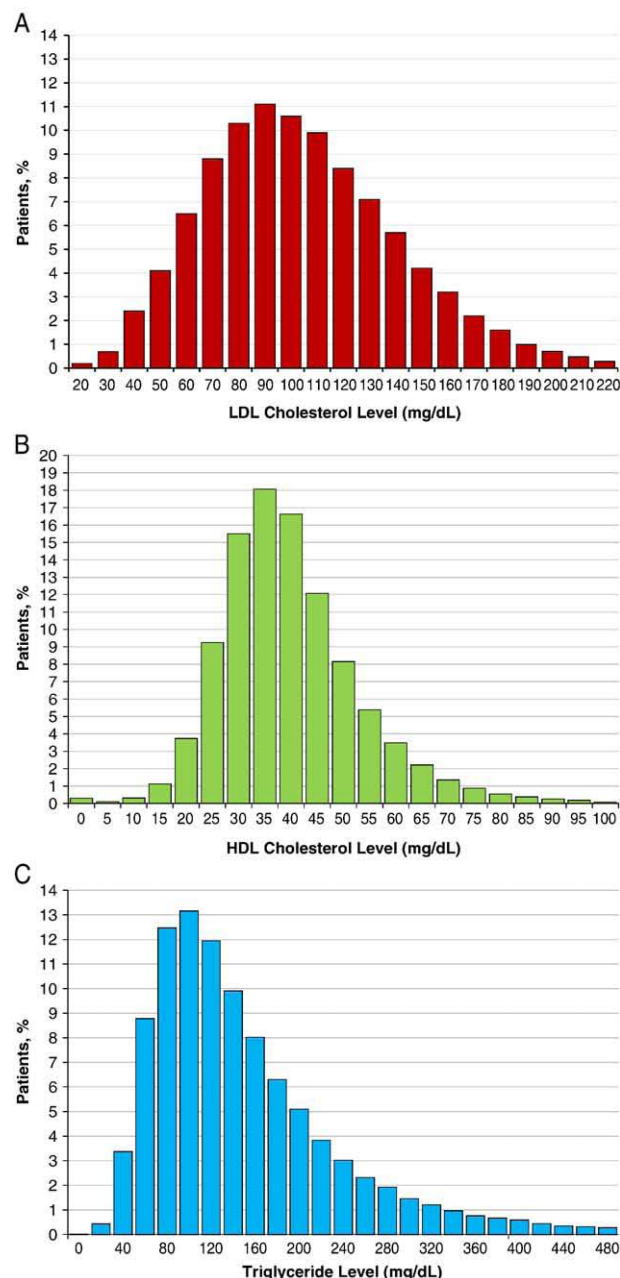
Table 1. Patient characteristics of the study population

Patient characteristics	Value
Age (y)	65 ± 14
Female	36.3%
Race/Ethnicity	
White	65.2%
Black	6.7%
Hispanic	5.7%
Asian	2.3%
Not documented	20.1%
Diagnosis	
STEMI/NSTEMI	75.0%
Unstable angina	4.5%
CAD	11.3%
Angina	13.1%
Prior myocardial infarction	16.5%
Peripheral vascular disease	6.6%
Prior Stroke	6.6%
Diabetes mellitus	26.2%
Prior CHD, other vascular disease, or diabetes	45.6%
Hypertension	54.2%
Hyperlipidemia history	35.5%
Prior use of lipid-lowering medications	21.1%
Smoking (current or prior 1 y)	30.4%
Renal insufficiency	6.5%
Renal dialysis (within past 3 mo)	1.3%
Chronic obstructive pulmonary disease	9.8%
History of atrial fibrillation	5.7%
Body mass index (kg/m ²)	28.9
Admission systolic blood pressure (mm Hg)	124.0 ± 20.9
Total cholesterol (mg/dL)	174.4 ± 47.7
LDL cholesterol (mg/dL)	104.9 ± 39.8
HDL cholesterol (mg/dL)	39.7 ± 13.2
Triglycerides (mg/dL)	161 ± 128

smokers. Prior MI was noted in 16.5% of patients. For this population, 45.6% had documented prior CHD, other atherosclerotic vascular disease, or diabetes, and 54.4% did not. Admission diagnoses were most commonly related to acute coronary events with 79% presenting with acute coronary syndromes (ST-segment elevation MI [STEMI]/non-ST-segment elevation MI [NSTEMI] 75.0%, unstable angina 4.5%). Other diagnoses included chest pain (rule out MI) in patient with prior CAD, CAD with or without stable angina, cerebral vascular disease, peripheral vascular disease, and subsequent care of MI. Before admission, 21.1% of patients were receiving lipid-lowering medications. Of patients with medical history of CAD, other atherosclerotic vascular disease, or diabetes, 29.4% were receiving lipid-lowering medications before admission compared to 14.2% of those without history of CAD, other atherosclerotic vascular disease, or diabetes who were receiving lipid-lowering medications ($P < .0001$).

For this hospitalized patient population with CAD, based on the lipid panel obtained within the first 24 hours of presentation, the mean LDL was 104.9 ± 39.8 mg/dL, mean HDL 39.7 ± 13.2 mg/dL, and mean triglycerides 161 ± 128 mg/dL. The distributions of admission LDL,

Figure 1



Distribution of admission LDL, HDL, and triglyceride levels. **(A)** Histogram of admission LDL levels in 10 mg/dL increments. **(B)** Histogram of admission HDL levels in 5 mg/dL increments. **(C)** Histogram of admission triglyceride levels in 20 mg/dL increments (truncated at 480 mg/dL).

HDL, and triglycerides are shown in Figure 1. Table II displays the distribution of categorized LDL levels in the study population. Half the patients hospitalized with CAD had admission LDL <100 mg/dL, and LDL <70 mg/dL was observed in 17.6% of patients. Less than one quarter of

Table II. Distribution of admission lipid levels**Total cohort**

HDL (mg/dL)	LDL (mg/dL)					Total (n = 103 632)
	<70 (n = 18 191)	70-99 (n = 33 111)	100-129 (n = 28 429)	130-159 (n = 15 385)	≥160 (n = 8516)	
<40 (n = 56 587)	10.8	17.8	14.7	7.6	3.8	54.6
40-59 (n = 38 883)	5.3	11.7	10.6	6.2	3.7	37.5
≥60 (n = 8162)	1.4	2.5	2.1	1.1	0.7	7.8
Total (n = 103 632)	17.6	32.0	27.4	14.9	8.2	100

Patients with history of CAD, other atherosclerotic vascular disease, or diabetes

HDL (mg/dL)	LDL (mg/dL)					Total (n = 55 539)
	<70 (n = 12 187)	70-99 (n = 19 173)	100-129 (n = 13 695)	130-159 (n = 6644)	≥160 (n = 3840)	
<40 (n = 31 590)	14.0	19.9	13.6	6.2	3.3	56.9
40-59 (n = 20 062)	6.5	12.3	9.4	4.9	3.0	36.1
≥60 (n = 3887)	1.5	2.4	1.7	0.8	0.6	7.0
Total (n = 55 539)	21.9	34.5	24.7	12.0	6.9	100

Patients without history of CAD, other atherosclerotic vascular disease, or diabetes

HDL (mg/dL)	LDL (mg/dL)					Total (n = 48 093)
	<70 (n = 6004)	70-99 (n = 13 938)	100-129 (n = 14 734)	130-159 (n = 8741)	≥160 (n = 4676)	
<40 (n = 24 997)	7.1	15.3	16.0	9.0	4.4	52.0
40-59 (n = 18 821)	4.0	11.0	12.0	7.7	4.4	39.1
≥60 (n = 4275)	1.3	2.7	2.6	1.4	0.9	8.9
Total (n = 48 093)	12.5	29.0	30.6	18.2	9.7	100

Values are expressed as percentage.

patients had an admission LDL >130 mg/dL. The distribution of patients by HDL categories is shown in Table II. There were 54.6% of patients hospitalized with CAD with admission HDL levels <40 mg/dL. HDL ≥60 was observed in just 7.8% of patients. Ideal levels (LDL <70 mg/dL and HDL ≥60 mg/dL) were observed in only 1.4% of patients hospitalized with CAD. Among patients with prior history of CAD, other atherosclerotic vascular disease, or diabetes, 56.4% had LDL <100 mg/dL and 21.9% had LDL <70 mg/dL (Table II). In these previously established patients with vascular disease or diabetes, admission HDL level were <40 mg/dL in 56.9%. Among those patients without prior history of CAD, other atherosclerotic vascular disease, or diabetes, 41.5% had LDL <100 mg/dL and 12.5% had LDL <70 mg/dL (Table II). Only 29.2% of the patients without prior history of atherosclerosis or diabetes had LDL ≥130 mg/dL. The distributions of patients by admission LDL and HDL categories for subgroups with and without STEMI/

NSTEMI, with and without prior MI, with and without prior lipid medication treatment, and with and without diabetes are shown in the Appendix A available online.

Among the 21.1% of patients receiving lipid-lowering medications before admission, LDL levels were modestly lower (94.3 ± 36.4 mg/dL) and HDL levels were similar to those not previously treated with lipid-lowering medications (39.6 ± 2.6 mg/dL). Of patients receiving lipid-lowering medications before admission, 64.0% had admission LDL <100 mg/dL and 24.5% had LDL <70 mg/dL (Appendix A available online). The LDL and HDL for patients presenting with acute coronary syndromes were 105.8 ± 39.7 and 39.5 ± 13.2 mg/dL, respectively, versus 101.7 ± 40.0 and 40.5 ± 13.3 mg/dL for patients with stable CAD diagnoses. Both LDL and HDL were slightly higher in women compared to men (106.3 ± 41.0 vs 104.2 ± 39.1 mg/dL, $P < .0001$, and 44.1 ± 14.5 vs 37.3 ± 11.8 mg/dL, $P < .0001$). Patients younger than 75 years had higher LDL levels and lower

Table III. Multivariable analysis—predictors of LDL levels*

Variable	GEE estimate	95% CI for GEE estimate		P
		Lower	Upper	
Female	6.0004	5.3153	6.6855	<.0001
Age (per 10 y increase)	−0.4476	−0.4751	−0.4201	<.0001
Presenting with acute coronary syndrome	3.1565	1.5128	4.8003	.0002
Prior MI	−5.4312	−6.0511	−4.8113	<.0001
History of dyslipidemia	4.3399	3.0963	5.5835	<.0001
Prior lipid-lowering medication	−13.7380	−14.9222	−12.5539	<.0001
History of hypertension	−3.3529	−3.9820	−2.7238	<.0001
History of diabetes	−7.7647	−8.4161	−7.1133	<.0001
History of renal insufficiency	−5.0092	−6.1317	−3.8868	<.0001
Body mass index, per 5 units increase	0.2468	0.2042	0.2894	<.0001
No history of smoking	−2.5216	−3.0713	−1.9719	<.0001

CI, Confidence interval.

*Negative estimate implies high level of the factor leads to low LDL, and positive estimate means high level of the factor leads to high LDL.

Table IV. Multivariable analysis—predictors of HDL levels*

Variable	GEE estimate	95% CI for GEE Estimate		P
		Lower	Upper	
Female	6.2098	5.9518	6.4677	<.0001
Age (per 10 y increase)	0.0633	0.0537	0.0730	<.0001
Presenting with acute coronary syndrome	−0.6317	−1.2272	−0.0361	.0376
Prior MI	−1.1643	−1.3653	−0.9632	<.0001
History of dyslipidemia	−0.5186	−0.7390	−0.2983	<.0001
Prior lipid-lowering medication	−0.0722	−0.3423	0.1978	.6001
History of hypertension	0.0609	−0.1237	0.2455	.5178
History of diabetes	−2.4910	−2.6777	−2.3043	<.0001
History of renal insufficiency	−1.4232	−1.7697	−1.0768	<.0001
Body mass index, per 5 units increase	−0.2034	−0.2191	−0.1877	<.0001
No history of smoking	1.6671	1.4150	1.9191	<.0001

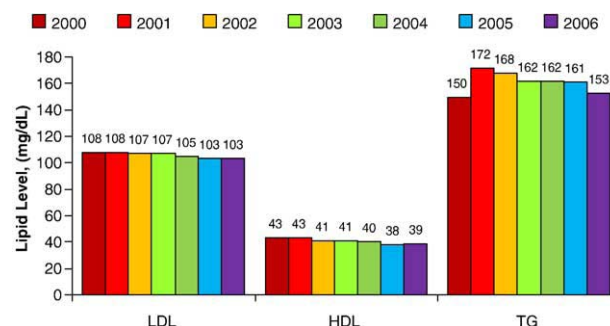
CI, Confidence interval.

*Negative estimate implies high level of the factor leads to low HDL, and positive estimate means high level of the factor leads to high HDL.

HDL levels (108.4 ± 40.6 vs 96.3 ± 36.3 mg/dL, $P < .0001$, and 38.7 ± 2.7 vs 42.5 ± 14.2 mg/dL, $P < .0001$).

Multivariable analyses were constructed to determine independent predictors of LDL levels as shown in Table III. Prominent predictors for higher LDL levels on admission included female gender, no diabetes, history of hyperlipidemia, no prior lipid-lowering therapy, and presenting with acute coronary syndrome. Multivariable analyses were also constructed for predictors of HDL levels as shown in Table IV. Lower HDL

Figure 2



Temporal trends in admission lipid levels 2000-2006. Admission levels for LDL, HDL, and triglycerides (mean) grouped by year from 2000-2006.

levels were associated with male gender and diabetes. Multivariable analyses for predictors of LDL ≥ 100 mg/dL and HDL < 40 mg/dL are shown in the Appendix A, available online.

Temporal trends in admission lipid levels were also studied as shown in Figure 2. Admission lipid levels were measured in 63%, 53%, 51%, 53%, 60%, 65%, and 71% of CAD hospitalizations from 2000 to 2006. During 2000 to 2006, there was a modest decline in LDL levels from 108 to 103 mg/dL, $P < .0001$. There was also a significant decline in HDL levels observed in this time frame, decreasing from 43 mg/dL in 2000 to 39 mg/dL in 2006 ($P < .0001$). From 2000 to 2006, there was a small increase in triglycerides levels from 150 to 153 mg/dL, $P < .0001$. Use of lipid-lowering medications before admission changed very little over time: 22.5% of patients in 2000 and 24.5% of patients in 2006. Body mass index increased over time from median of 27.7 in 2000 to 28.2 kg/m² in 2006, $P < .0001$. The temporal trends in admission LDL, HDL, and triglyceride levels were similar in patients receiving and not receiving lipid medications before admission. After adjusting for multiple patient characteristics predictive of lipid levels including use of lipid-lowering medications before admission, the temporal trends observed in both LDL and HDL remained statistically significant.

Discussion

Numerous studies have demonstrated that total cholesterol and LDL are major modifiable risk factors for atherosclerotic vascular disease and its clinical manifestations. Prospective epidemiological data have suggested that the relationship between LDL and CHD is log-linear, with a relative risk set at 1.0 for LDL of 40 mg/dL.² A large number of randomized clinical trials have demonstrated that lowering LDL with certain lipid-lowering medications reduces the risk of first or recurrent cardiovascular

events.¹ On the basis of accumulated evidence from epidemiological studies and randomized controlled trials, NCEP guidelines have identified LDL as the primary target of cholesterol-lowering therapy and recommended a treatment algorithm for initiating LDL-lowering therapy. Recent major clinical trials, including the Pravastatin or Atorvastatin Evaluation Infection Therapy-Thrombolysis In Myocardial Infarction as well as Treat to New Targets have supported even lower treatment targets for LDL in secondary prevention patients.^{5,6} As a result of these data, the Adult Treatment Panel III guidelines were revised in 2004 to include an optional therapeutic goal of LDL <70 mg/dL in high-risk patients.²

Although high serum concentrations of LDL are a major risk factor for CHD, patients may present with CAD events despite LDL levels, which are not considered elevated and fall well within guideline-recommended targets. In the present study, almost half of patients hospitalized with CAD have admission LDL <100 mg/dL, and 17.6% of patients had LDL <70 mg/dL. Even when only patients without prior history of CHD, other atherosclerotic vascular disease, or diabetes were studied, 72.1% have admission LDL <130 mg/dL and 41.5% had LDL <100 mg/dL. Thus, a substantial proportion of patients present with their first or recurrent CHD events well within the current guideline-recommended targets for LDL. In addition, a large proportion of the patients included in this study could reach the standard and optional NCEP LDL goals without statin therapy or with statin doses lower than any shown to be most effective in clinical trials.⁵ Given that clinical trials have shown high-intensity statin therapy to be effective irrespective of starting LDL level, these data suggest that NCEP guidelines should further integrate risk reduction targeting in addition to LDL goals.

Many of these patients presenting with CAD had HDL levels, which are associated with excess risk. High-density lipoprotein cholesterol is inversely related to the risk of CAD.⁷ Even modest increases are associated with lower risk for nonfatal MI or death from CHD.⁸ There were 54.6% of patients hospitalized with CAD with admission HDL <40 mg/dL. In addition, fewer than 10% of patients had HDL ≥60 mg/dL. Ideal levels (defined as LDL <70 mg/dL and HDL ≥60 mg/dL) were present in only 1.4% of patients hospitalized with CAD. For further reduction in cardiovascular risk, it may be necessary to identify and implement therapies that increase antiatherogenic HDL.

The guidelines recommend obtaining a lipid panel within 24 hours of presentation in patients hospitalized with a cardiovascular event or for a cardiovascular procedure.^{1,2}

In this study population, lipid levels were obtained in only 59% of patients hospitalized with CAD. Although clinicians may empirically treat with lipid-lowering medications, measuring admission lipid levels remain guideline-recommended because admission lipid levels may influence treatment decisions, including intensifica-

tion of therapy for those previously treated with lipid-lowering medications.¹

A number of genetic, disease state, and lifestyle factors have been shown to be related to lipid levels in adults, including dietary intake of saturated fat and cholesterol, excess weight, and level of physical activity. Among patients hospitalized with CAD assessed in this study, as expected, a history of hyperlipidemia and no prior lipid-lowering therapy were both associated with higher LDL levels. Female gender was also associated with higher LDL, a finding which contradicts prior studies.¹ Male gender was associated with lower HDL, as was history of diabetes, both findings concordant with prior studies of the metabolic syndrome.⁹

Cholesterol levels in patients with CAD have declined since the 1960s, first markedly, and in more recent years in a more gradual fashion.¹⁰ Analysis of the NHANES (National Health and Nutrition Examination Survey) database since 1960 reveals that the percentage reporting high cholesterol levels decreased from 33.5% in 1960-1962 to 20.8% in 1988-1994, and then increased to 22.5% in 1999-2000.¹⁰ A more recent analysis of NHANES demonstrated that between 1988-1994 and 1999-2002, total serum cholesterol level of adults aged 20 years or older decreased from 206 to 203 mg/dL and LDL levels decreased from 129 to 123 mg/dL.⁵ There were greater decreases in LDL observed in men 60 years or older and in women 50 years or older. During this period, there was no change in mean HDL levels and nonsignificant increases in mean serum triglyceride levels. The present study demonstrates that among patients hospitalized with CAD, the admission lipid levels are below that of the general population. The lower admission LDL levels among patients hospitalized with CAD compared to the general population may be the result of shifts in the prevalence of other cardiovascular risk factors, differences in use of lipid-lowering therapy, or other factors and is deserving of further study. This study also demonstrates a decrease in admission LDL and HDL levels over the 2000-to-2006 time frame. The finding of a 10% decrease in admission HDL levels over the 6-year period is quite notable and may reflect increasing rates of obesity, insulin resistance, and diabetes.

A substantial proportion of patients fail to remain on lipid-lowering medication treatment during outpatient follow-up. In the present study, only 21.1% of patients were receiving lipid-lowering therapy before hospitalization despite almost half having prior history of CAD, other atherosclerotic vascular disease, or diabetes before hospitalization. Among patients in the NCEP Evaluation Project Utilizing Novel E-Technology II Survey trial, which assessed treatment success under the ATP III guidelines, 67% had achieved their LDL goal, and 62% of those with CHD had a LDL cholesterol concentration of <100 mg/dL.¹¹ Although this is a marked improvement from the previous national survey (The Lipid Treatment

Assessment Program),¹² these studies recruited investigators who are among the highest prescribers of statins, and as a result, likely overestimate the probability of treatment success in the community. The present study selects a broader population of patients. Assessing the frequency of lipid-lowering therapy on admission, rather than at discharge or during the hospitalization, provides evidence suggesting that a substantial proportion of high-risk patients (CHD or CHD risk equivalents) are not receiving lipid-lowering drugs on an outpatient basis. Their admission for CAD can be viewed as having resulted, in part, from failure to have successfully implemented and maintained secondary prevention measures.

Study limitations

There is the potential for selection bias in this study because admission lipid levels were not measured in 41% of patients, and there were modest baseline differences between those with and without admission lipid levels, which may influence the generalizability of these findings. There is some evidence that as a part of the acute phase response, lipid metabolism is significantly altered in patients with unstable coronary syndromes.^{13,14} Although it has been reported that a decrease in total cholesterol and LDL takes place during the acute phase of MI, with a marked fall occurring 24 hours after infarction and lasting up to 12 days, a recent study found little change in lipid levels when measured serially in the first 4 days of an acute coronary syndrome event hospitalization.¹⁵ Although the lipid levels obtained in this study were measured in the first 24 hours of admission, they may or may not be entirely reflective of the baseline steady state lipid levels. Further, we do not have data as to whether patients were in the fasting state. This real-world study used results of various commercially available lipid panel assays rather than results from a single central core laboratory. Although this methodology may introduce great variability to lipid testing results, this approach makes these findings more applicable to clinical practice. Specific medications prescribed before admission and doses were not available in this study. It must also be considered that these findings may not apply to patients who present with CAD in hospital settings that deviate substantially from those in GWTG.

Conclusions

In a large cohort of patients hospitalized with CAD, almost half have admission LDL <100 mg/dL, whereas less than a quarter have LDL >130 mg/dL. The LDL levels <70 mg/dL are observed in only 17.6% of patients. Admission HDL levels are <40 mg/dL in 54.6% of patients hospitalized with CAD, whereas <10% of patients have admission HDL levels ≥60 mg/dL. Ideal lipid levels (LDL <70 mg/dL with HDL ≥60 mg/dL) are seen in only 1.4% of

patients hospitalized with CAD. There were reductions in admission LDL and HDL levels over time. These findings provide insights into the lipid levels encountered in recent clinical practice for patients hospitalized with CAD. These findings may provide further support for recent guideline revisions with even lower LDL goals. They also may suggest a clinical need for developing effective treatments to raise antiatherogenic HDL.

References

1. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). 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) Final Report. *Circulation* 2002;106:3143-421.
2. Grundy SM, Cleeman JJ, Merz CNB, et al, for the Coordinating Committee of the National Cholesterol Education Program and Endorsed by the National Heart, Lung, and Blood Institute, American College of Cardiology Foundation, and American Heart Association. Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. *Circulation* 2004;110:227-39.
3. Carroll MD, Lacher DA, Sorlie PD, et al. Trends in serum lipids and lipoproteins of adults, 1960-2002. *JAMA* 2005;294:1773-81.
4. LaBresh KA, Ellrodt AG, Gliklich R, et al. Get With The Guidelines for cardiovascular secondary prevention: pilot results. *Arch Intern Med* 2004;164:203-9.
5. Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med* 2004;350:1495-504.
6. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;360:7-22.
7. Castelli W. Cholesterol and lipids in the risk of coronary artery disease—the Framingham Heart Study. *Can J Cardiol* 1988;4 (Suppl A):5a-10a.
8. Ansell BJ, Watson KE, Fogelman AM, et al. High-density lipoprotein function: recent advances. *J Am Coll Cardiol* 2005;46:1792-8.
9. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet* 2005;365:1415-28.
10. Gregg EW, Cheng YJ, Cadwell BJ, et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. *JAMA* 2005;293:1868-74.
11. Davidson MH, Maki KC, Pearson TA, et al. Results of the National Cholesterol Education (NCEP) Program Evaluation Project Utilizing Novel E-Technology (NEPTUNE) II Survey and Implications for Treatment Under the Recent NCEP Writing Group Recommendations. *Am J Cardiol* 2005;96:556-63.
12. Pearson TA, Laurora I, Chu H, et al. The Lipid Treatment Assessment Project (L-TAP): a multicenter survey to evaluate the percentages of dyslipidemic patients receiving lipid-lowering therapy and achieving low-density lipoprotein cholesterol goals. *Arch Intern Med* 2000;160:459-67.
13. Dodds C, Mills GL. Influence of myocardial infarction on plasma-lipoprotein concentration. *Lancet* 1959;1:1160-3.
14. Pfohl M, Schreiber I, Liebich HM, et al. Upregulation of cholesterol synthesis after acute myocardial infarction—is cholesterol a positive acute phase reactant? *Atherosclerosis* 1999;142:389-93.
15. Pitt B, Loscalzo J, Ycas J, et al. Lipid levels after acute coronary syndromes. *J Am Coll Cardiol* 2008;51:1440-5.

Appendix A

Table A1. Distribution of admission lipid levels among patient subgroups

Patients with NSTEMI/STEMI

HDL (mg/dL)	LDL (mg/dL)					Total (n = 31 461)
	<70 (n = 7528)	70-99 (n = 10 752)	100-129 (n = 7519)	130-159 (n = 3496)	≥160 (n = 2166)	
<40 (n = 40 113)	10.33	17.67	15.48	8.20	4.14	55.81
40-59 (n = 26 247)	5.01	11.01	10.28	6.39	3.83	36.52
≥60 (n = 5509)	1.39	2.39	2.03	1.09	0.77	7.67
Total (n = 71 869)	16.73	31.07	27.79	15.68	8.74	100.00

Patients without NSTEMI/STEMI

HDL (mg/dL)	LDL (mg/dL)					Total (n = 26 053)
	<70 (n = 5190)	70-99 (n = 8828)	100-129 (n = 6736)	130-159 (n = 3406)	≥160 (n = 1893)	
<40 (n = 13 613)	12.19	17.96	12.82	6.14	3.14	52.25
40-59 (n = 10 233)	6.22	13.15	10.75	5.76	3.40	39.28
≥60 (n = 2207)	1.51	2.78	2.28	1.17	0.73	8.47
Total (n = 26 053)	19.92	33.88	25.85	13.07	7.27	100.00

Patients with prior myocardial infarction

HDL (mg/dL)	LDL (mg/dL)					Total (n = 20 054)
	<70 (n = 4794)	70-99 (n = 7250)	100-129 (n = 4622)	130-159 (n = 2180)	≥160 (n = 1208)	
<40 (n = 11 739)	15.56	21.04	12.80	5.97	3.17	58.54
40-59 (n = 7022)	6.91	12.78	8.70	4.23	2.40	35.02
≥60 (n = 1293)	1.43	2.33	1.56	0.67	0.46	6.45
Total (n = 20 054)	23.91	36.15	23.05	10.87	6.02	100.00

Patients without prior myocardial infarction

HDL (mg/dL)	LDL (mg/dL)					Total (n = 79 938)
	<70 (n = 13 026)	70-99 (n = 24 865)	100-129 (n = 22 657)	130-159 (n = 12 484)	≥160 (n = 6906)	
<40 (n = 42 907)	9.84	17.07	15.05	7.82	3.89	53.68
40-59 (n = 30 446)	5.03	11.46	11.08	6.59	3.93	38.09
≥60 (n = 6585)	1.42	2.58	2.21	1.20	0.82	8.24
Total (n = 79 938)	16.30	31.11	28.34	15.62	8.64	100.00

Patients with diabetes

HDL (mg/dL)	LDL (mg/dL)					Total (n = 31 461)
	<70 (n = 7528)	70-99 (n = 10 752)	100-129 (n = 7519)	130-159 (n = 3496)	≥160 (n = 2166)	
<40 (n = 18 817)	15.82	20.82	14.02	5.92	3.23	59.81
40-59 (n = 10 784)	6.63	11.46	8.67	4.48	3.05	34.28
≥60 (n = 1860)	1.48	1.90	1.21	0.72	0.60	5.91
Total (n = 31461)	23.93	34.18	23.90	11.11	6.88	100.00

Table A1 (continued)

Patients with diabetes

HDL (mg/dL)	LDL (mg/dL)					Total (n = 68 531)
	<70 (n = 10 292)	70-99 (n = 21 363)	100-129 (n = 19 760)	130-159 (n = 11 168)	≥160 (n = 5948)	
<40 (n = 35 829)	8.77	16.51	14.86	8.16	3.98	52.28
40-59 (n = 26 684)	4.85	11.85	11.49	6.87	3.88	38.94
≥60 (n = 6018)	1.40	2.82	2.48	1.27	0.81	8.78
Total (n = 68 531)	15.02	31.17	28.83	16.30	8.68	100.00

Table A2. Multivariable analysis—predictors of LDL and HDL Levels

Variable	Odds ratio	95% CI for adjusted OR		P
		Lower	Upper	
Odds of LDL ≥100 mg/dL				
Female	12.7884	3.48393	46.9424	.00012
Age (per 10 year increase)	1.0303	0.99778	1.0639	.06811
Presenting with ACS	0.4074	0.17447	0.9512	.03793
Prior MI	1.8408	0.72943	4.6455	.19637
History of dyslipidemia	0.2973	0.09401	0.9400	.03889
Prior lipid lowering medication	0.2172	0.03101	1.5220	.12427
History of hypertension	0.5878	0.27005	1.2795	.18063
History of diabetes	1.2485	0.51808	3.0088	.62089
History of renal insufficiency	0.5456	0.07866	3.7845	.53981
Body mass index, per 5 units increase	0.9430	0.87451	1.0168	.12672
No history of smoking	0.9611	0.43249	2.1359	.92247
Odds of HDL <40 mg/dL				
Female	0.96542	0.91570	1.01785	.19219
Age (per 10 year increase)	0.99388	0.99137	0.99639	<.00001
Presenting with ACS	0.80545	0.71423	0.90831	.00042
Prior MI	1.11349	1.05955	1.17018	.00002
History of dyslipidemia	1.01406	0.96038	1.07074	.61496
Prior lipid lowering medication	1.10042	1.04402	1.15987	.00036
History of hypertension	1.05521	1.01391	1.09818	.00833
History of diabetes	1.56304	1.48155	1.64901	<.00001
History of renal insufficiency	1.36466	1.26896	1.46758	<.00001
Body mass index, per 5 units increase	1.00437	1.00117	1.00758	.00747
No history of smoking	0.93645	0.89564	0.97912	.00388