Incidence of and Factors Associated with Achieving Target Lipid Levels in Patients with Peripheral Arterial Disease

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BACKGROUND: Patients with peripheral arterial disease (PAD) have increased mortality compared with patients without PAD. Coronary artery disease (CAD) accounts for almost 75% of deaths in PAD patients. Studies suggest that PAD is underdiagnosed and atherosclerotic risk factors undertreated when compared with CAD.

OBJECTIVE: To determine whether cholesterol guidelines are being met in patients with PAD and to determine whether any independent factors increase the likelihood of reaching goal low-density lipoprotein (LDL).

DESIGN: A retrospective chart review of subjects diagnosed with PAD in 2001 at 2 Veterans Affairs Medical Centers.

MEASUREMENTS: Univariate analysis compares baseline characteristics between those reaching goal and those who do not. Multivariate logistic regression analysis identified predictors of meeting LDL goal among PAD patients.

RESULTS: Of 315 patients, 62% reached goal LDL. Those more likely to reach goal were older, had hypertension, and a history of CAD and stroke. Positive predictors of LDL goal were age and CAD, while smoking was a negative predictor.

CONCLUSION: The majority of veterans with PAD received lipid-lowering medication and achieve goal LDL, but they are more likely to do so if they are older than 70 and have a history of CAD.

KEY WORDS: hyperlipidemia; peripheral arterial disease; coronary artery disease.

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Peripheral arterial disease (PAD) is a progressive condition characterized by abnormal blood flow to the lower extremities. It affects an estimated 27 million people above 55 years of age in North America and Europe. As an indicator of disease severity, a U.S. disease-based data set used to compare 5-year mortality rates from common malignancies demonstrated that the patient survival rate for severe PAD is poorer than survival for breast cancer and Hodgkin's disease.^{1,2}

Less than 40% (only 10.5 million) of patients with PAD are symptomatic.³ Symptoms range in severity from intermittent claudication to critical limb ischemia, which can progress to nonhealing wounds and gangrene with resultant need for amputation. An indicator of systemic atherosclerosis, PAD often occurs in concert with coronary artery disease (CAD) and cerebrovascular disease. Patients with PAD have an increased

risk of atherothrombotic events and are 6 times more likely to die within 10 years than patients without PAD.⁴ Coronary artery disease is the leading cause of death in patients with PAD, accounting for almost 75% of deaths.⁵ Because of this strong association between PAD and CAD mortality, the American Heart Association and National Cholesterol Education Program (NCEP) recommend aggressive atherosclerotic risk factor therapy for patients with PAD, including a goal low-density lipoprotein (LDL) cholesterol level of less than 100 mg/dL.^{6,7} As this study was conducted, the NCEP has recommended an even lower LDL goal (<70 mg/dL) in certain high-risk populations.⁸

Evidence supports the current guidelines to treat atherosclerotic risk factors aggressively. In a randomized, placebo-controlled trial of over 20,000 high-risk patients (history of CAD, DM, stroke, or PAD) randomized to either a lipid-lowering agent (an HMGCoA-reductase inhibitor) or placebo, those patients randomized to the treatment arm had a 25% reduction in cardiovascular events compared with placebo. In a subset of patients with PAD (those with intermittent claudication or reporting a history of having a procedure for PAD) without CAD, similar results were found.⁹ Furthermore, the Cochrane Library reports that in patients with claudication, lipid-lowering therapy reduces disease progression and claudication.¹⁰ Studies suggest that PAD is underdiagnosed and associated risk factors undertreated when compared with CAD.¹¹⁻¹⁵

OBJECTIVE

The purpose of this study is to determine whether current cholesterol guidelines are being met in patients with PAD and whether any independent factors increase the likelihood of reaching goal LDL.

DESIGN AND SUBJECTS

The setting for the study was the Miami Veterans Affairs Medical Center (VAMC) located in Miami, FL, and affiliated with the University of Miami Miller School Of Medicine and the West Haven VAMC located in West Haven, CT, and affiliated with Yale University School of Medicine.

Eligible subjects were patients diagnosed with PAD, defined as an ankle brachial index (ABI: ankle systolic blood pressure/the higher brachial systolic blood pressure) of less than 1 in either extremity, by a noninvasive vascular study during 2001 who had at least 1 year of documented follow-up. Via a detailed retrospective electronic chart review, data were

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extracted on patient demographics, weight, blood pressure, comorbid conditions/symptoms (e.g., diabetes mellitus, CAD, hypertension, cerebrovascular disease, claudication), vascular procedures, medications, smoking history, and certain laboratory results. When more than 1 blood pressure, hemoglobin A1c, or LDL cholesterol was obtained, we used the value closest to 12 months post-ABI for analysis. Subjects who died within 1 year of noninvasive testing, had no LDL data ($n=9$), or were followed for lipid management at another institution as documented in progress notes of the patient record ($n=2$) were excluded from analysis. Some Connecticut subjects were reported previously in a pilot study.¹⁶ One author, M.B., not involved in the clinical care of any of the included patients, reviewed the medical record data using standard definitions and an abstraction tool developed for the study.

The primary outcome was LDL cholesterol. For the multivariate modeling, we defined being at goal as an LDL cholesterol of $<100\text{mg/dL}$ and not being at goal as an LDL cholesterol of $\geq 100\text{mg/dL}$. We recorded both left and right lower extremity ABIs. However, for some analyses, we used the minimum ABI, the lower of these 2 values.

MEASUREMENTS

We used descriptive statistics to summarize baseline demographic and clinical characteristics by achieving LDL goal. We used Student's *t*-test for continuous variables and the χ^2 test (or Fisher's exact test if an expected number in any cell was less than 5) for discrete variables to determine whether the baseline characteristics were different between those meeting and those not meeting the LDL goal.

We performed multivariate logistic regression analysis to identify predictors of meeting LDL goal among peripheral vascular disease (PVD) patients. We included in the model the independent variables on the basis of a priori clinical judgment (e.g., history of diabetes mellitus or myocardial infarction) as well as of the distributions of baseline characteristics by reaching the LDL goal. We used the backward selection method in determining the final model.

All analyses were performed using the SAS systems for Windows v8 (SAS Institute, Cary, NC). A 2-sided significance level of .05 was used for all tests.

RESULTS

The basic demographic and clinical characteristics by reaching the LDL goal are presented in Table 1. A total of 315 patients were included in the present analysis, among whom 62% reached LDL goal. Univariate analyses showed that PAD patients who met LDL goal were older (mean $\pm$ SD: 71 ± 10 vs 66 ± 11 , $P<.01$) and had hypertension (64% vs 42%, $P=.01$), a history of CAD (69% vs 50%, $P<.01$), and a history of stroke (70% vs 57%, $P=.03$). Current smokers were less likely to meet the LDL goal than nonsmokers (47% vs 68%, $P<.01$) as were patients using PAD medications (53% vs 70%, $P<.01$). The proportion of PAD patients with claudication who met the LDL goal was lower than patients without claudication, but the difference did not reach significance (59% vs 69%, $P=.09$). Compared with Hispanics (37%), Caucasians (61%) and African Americans (69%) appeared more likely to achieve the LDL goal, but the differences were not statistically significant ($P=.08$).

Table 1. Basic Demographic and Clinical Characteristics of the Study Population*

	LDL < 100 ($n=194$) <i>n</i> (%)	LDL ≥ 100 ($n=121$) <i>n</i> (%)	<i>P</i> Value
Age (mean $\pm$ SD)	71 $\pm$ 10	66 $\pm$ 11	$<.01$
Weight	179 $\pm$ 37	183 $\pm$ 38	.32
Race			
White	134 (61)	87 (39)	.08
Black	33 (69)	15 (31)	
Hispanic	7 (37)	12 (63)	
Other	17 (71)	7 (29)	
Claudication			
Yes	131 (59)	93 (41)	.09
No	62 (69)	28 (31)	
Diabetes			
Yes	97 (63)	58 (37)	.72
No	97 (61)	63 (39)	
Hypertension			
Yes	177 (64)	100 (36)	.01
No	15 (42)	21 (58)	
CAD			
Yes	135 (69)	62 (31)	$<.01$
No	58 (50)	59 (50)	
Stroke			
Yes	80 (70)	35 (30)	.03
No	113 (57)	86 (43)	
PVD procedure			
Yes	52 (55)	43 (45)	.10
No	142 (65)	78 (35)	
PVD medication			
Yes	82 (53)	74 (47)	$<.01$
No	112 (70)	47 (30)	
PVD severity			
ABI ≤ 0.4	37 (61)	24 (39)	.90
$0.4 < \text{ABI} \leq 0.7$	66 (62)	43 (38)	
$0.7 < \text{ABI} \leq 0.9$	68 (61)	43 (39)	
ABI > 0.9	23 (68)	11 (32)	
Current smoker			
Yes	48 (47)	54 (53)	$<.01$
No	145 (68)	67 (32)	

*Column totals may not add up due to missing data.

PVD, peripheral vascular disease; ABI, ankle brachial index; LDL, low-density lipoprotein.

Weight, PAD severity, and diabetes were not associated with meeting the LDL goal.

An examination of whether meeting the LDL target was associated with patients taking lipid-lowering drugs was performed, and the results are shown in Table 2. We found that 44% of the patients not prescribed lipid-lowering drugs did not meet the LDL target, while the figure was 37% for patients prescribed lipid-lowering drugs. The difference, however, was not statistically significant ($P=.28$).

The results from multivariate logistic regression backward selection are shown in Table 3. Variables of ABI, diabetes, stroke, hypertension, and race (Hispanics vs non-Hispanics) were eliminated from the model. The final predictors of the LDL goal included age (odds ratio [OR]=1.03; 95% confidence interval [CI]: 1.01 to 1.06), CAD (1.86, 1.13 to 3.05), claudication (0.57; 0.33 to 0.99), and current smoking (0.53; 0.32 to 0.89). Older patients and patients with CAD were more likely to meet the LDL goal, while current smoking and claudication were associated with lower proportions of meeting the LDL goal.

Table 2. LDL Target Status by Prescription of the Lipid-Lowering Drugs*

	Not Prescribed N (%)	Prescribed N (%)
LDL target not met (n=121)	34 (43.6)	87 (36.7)
LDL target met (n=194)	44 (56.4)	150 (63.3)

* $P=.28$ (χ^2 test).

LDL, low-density lipoprotein.

DISCUSSION

While the benefit of lipid-lowering therapy in atherosclerotic disease has been extensively investigated and accepted, most of the attention has been given to CAD. In a study to assess implementation of secondary prevention guidelines in patients hospitalized with carotid disease and PAD, 30% of patients had a total cholesterol level greater than 200 mg/dL; LDL cholesterol was not reported. Lipid-lowering medication was prescribed in one-third of the patients, but those with carotid disease were more likely than those with extremity disease to be on it.¹⁷ A recent investigation of 105 patients admitted for peripheral vascular surgery reported that 85 had lipid profiles recorded in the chart and only 42% of these were at or below the goal of less than 100 mg/dL for LDL.¹⁸ These reports include atherosclerotic patients without selecting for PAD alone.

The limited data available on current lipid management of PAD without a CAD diagnosis in the United States and Canada report a less than 50% treatment rate.^{19–20} In a cohort of 1,733 patients with PAD and no diagnosis of CAD, 31.3% were receiving a statin, 6% had screening fasting lipid profiles, and 44% had an LDL cholesterol of less than 100 mg/dL.

We found significantly higher treatment and success rates with 75% of PAD patients receiving cholesterol-lowering drugs and, overall, 62% reaching the goal LDL. Prescribed medicines included the fibrate gemfibrozil, niacin, and/or the most commonly used lipid-modifying drug prescribed in our study, simvastatin. Although we found that more patients prescribed cholesterol medicines achieved goal versus those not, the numbers did not reach statistical significance. Nine patients were excluded because of lack of LDL data.

Patients with PAD who had concomitant CAD were more likely to achieve goal LDL than patients with PAD without CAD, suggesting that physicians and patients both place greater significance on “heart attacks” and heart disease than on peripheral vascular disease. As a result, they may treat atherosclerotic risk factors such as dyslipidemia more aggressively in these patients. Furthermore, we found CAD to be an independent predictor of achieving goal LDL. We also found that older age and not smoking were predictive of reaching the target lipid level. Older patients (age > 70 years) more often met the goal than younger patients. This may be due to the recog-

nition of mortality in this older population and perhaps increased compliance. Current smokers are half as likely to reach the goal, suggesting either noncompliance, health care provider under treatment with either medications or therapeutic lifestyle interventions, or an accelerated, recalcitrant atherosclerotic process.

Additionally, while race was not a statistically significant factor in predicting target lipid level attainment, we did find that white and black patients met LDL goal more often than Hispanics. Whether this is due to patient compliance, less aggressive treatment, or physiologically recalcitrant disease in this patient population is also not known.

Previous studies have shown that the risk of cardiovascular death increases with increasing severity of PAD.²¹ Interestingly, we did not find an association between PAD severity and reaching goal. It does not seem that clinicians are more aggressive or successful in treating this susceptible population.

LIMITATIONS

Our study has limitations. The overwhelming majority of patients receiving care at Veterans Affairs Hospitals are white males. Whether our results can be generalized to other populations is not clear. The Veterans Affairs Hospitals have an electronic medical record allowing all health care providers within the VA system access to progress notes, laboratory results, and other ancillary testing. This electronic database prompts physicians to check certain blood tests, offer vaccinations, and conduct certain screening exams as part of quality improvement initiatives implemented in the 1990s.

Chart reviews draw conclusions from medical records. While prescribed medicines are known, compliance with prescriptions is not. Additionally, we identified patients who underwent diagnostic vascular testing. We do not know whether patients with PAD who are not referred for diagnostic testing are more or less likely to reach the goal LDL.

CONCLUSION

Our results demonstrate that the majority of patients in our study with PAD receive lipid-lowering medication and achieve the goal LDL. They are more likely to do so if they are older than 70 years and have a history of CAD, and less likely if they currently smoke. Knowing the need for aggressive atherosclerotic risk factor management in patients with PAD, we have identified areas where there are opportunities for improvement.

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Table 3. Multivariate Logistic Regression on Predictors of Low-Density Lipoprotein < 100 in Pulmonary Vascular Disease Patients—Backward Elimination Method

	Odds Ratio	95% Confidence Interval	P-Value
Age	1.03	1.01 to 1.06	.01
Coronary artery disease	1.86	1.13 to 3.05	.01
Claudication	0.57	0.33 to 0.99	.05
Current smoker	0.53	0.32 to 0.89	.02

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