Influence of Low HDL on Progression of Coronary Artery Disease and Response to Fluvastatin Therapy

Christie M. Ballantyne, MD; J. Alan Herd, MD; Laura L. Ferlic, MS; J. Kay Dunn, PhD; John A. Farmer, MD; Peter H. Jones, MD; Jeffrey R. Schein, DrPH; Antonio M. Gotto, Jr, MD, DPhil

Background—Patients with coronary artery disease (CAD) commonly have low HDL cholesterol (HDL-C) and mildly elevated LDL cholesterol (LDL-C), leading to uncertainty as to whether the appropriate goal of therapy should be lowering LDL-C or raising HDL-C.

Methods and Results—Patients in the Lipoprotein and Coronary Atherosclerosis Study (LCAS) had mildly to moderately elevated LDL-C; many also had low HDL-C, providing an opportunity to compare angiographic progression and the benefits of the HMG-CoA reductase inhibitor fluvastatin in patients with low versus patients with higher HDL-C. Of the 339 patients with biochemical and angiographic data, 68 had baseline HDL-C <0.91 mmol/L (35 mg/dL), mean 0.82±0.06 mmol/L (31.7±2.2 mg/dL), versus 1.23±0.29 mmol/L (47.4±11.2 mg/dL) in patients with baseline HDL-C ≥0.91 mmol/L. Among patients on placebo, those with low HDL-C had significantly more angiographic progression than those with higher HDL-C. Fluvastatin significantly reduced progression among low–HDL-C patients: 0.065±0.036 mm versus 0.274±0.045 mm in placebo patients (P=0.0004); respective minimum lumen diameter decreases among higher–HDL-C patients were 0.036±0.021 mm and 0.083±0.019 mm (P=0.09). The treatment effect of fluvastatin on minimum lumen diameter change was significantly greater among low–HDL-C patients than among higher–HDL-C patients (P=0.01); among low–HDL-C patients, fluvastatin patients had improved event-free survival compared with placebo patients.

Conclusions—Although the predominant lipid-modifying effect of fluvastatin is to decrease LDL-C, patients with low HDL-C received the greatest angiographic and clinical benefit. (Circulation. 1999;99:736-743.)

Key Words: angiography ■ cholesterol ■ coronary disease ■ drugs ■ lipoproteins

Clinical Investigation and Reports
otherwise indicated, patients were analyzed by randomized treatment, ie, fluvastatin or placebo. The primary endpoint was within-patient per-lesion change in minimum lumen diameter (MLD) of qualifying lesions as assessed by quantitative coronary angiography at baseline and 2.5-year follow-up.

**Patients**

Men and postmenopausal women aged 35 to 75 years with angiographic evidence of CAD and LDL-C of 2.97 to 4.91 mmol/L (115 to 190 mg/dL) on the NCEP Step I diet were eligible. Angiographic criteria included ≥1 atherosclerotic lesion causing ≥30% to 75% diameter stenosis by caliper measurement in a coronary artery untreated by PTCA and not 100% occluded and at least 2 of the 3 major coronary arteries untreated by PTCA, not 100% occluded, and evaluable by angiography. Patients were not excluded for prior myocardial infarction (MI) at least 6 months before randomization. Exclusion criteria included mean fasting plasma triglyceride ≥2.82 mmol/L (250 mg/dL) in patients assigned cholesterolamine or >3.39 mmol/L (300 mg/dL) in any patient, diabetes mellitus requiring insulin or an oral hypoglycemic agent, fasting blood glucose >9.4 mmol/L (170 mg/dL), uncontrolled hypertension, prior CABG, atherectomy, and coronary stent.

**Lipids, Apolipoproteins, and Coagulation Factors**

Lipid, apolipoprotein, and coagulation factor concentrations were assessed in fasting blood samples drawn at weeks –2, 0, 54, and 130 by a laboratory certified by the US National Heart, Lung, and Blood Institute/Centers for Disease Control and Prevention Part III Program (Medical Research Laboratories) as previously described.

**Quantitative Coronary Angiography**

The Cardiovascular Angiography Analysis System was used for angiographic assessment at baseline (1 to 16 weeks before randomization) and at final follow-up (as close to week 130 as possible; angiography required for clinical reasons could be substituted if evaluable for analysis and performed ≥1 year after randomization). All patients received 0.4 mg sublingual nitroglycerin unless medically contraindicated. Lesions qualifying for the primary analysis had MLD ≥25% of the reference lumen diameter at baseline and MLD at least 0.8 mm less than the reference lumen diameter at either baseline or follow-up. Lesions were excluded from the analysis if they were poorly visualized at baseline or follow-up, had reference lumen diameter <1.5 mm at baseline, or were in arteries treated by PTCA or with total occlusion at baseline.

**Clinical Events**

Clinical events were defined as PTCA, CABG, definite or probable MI, unstable angina pectoris requiring hospitalization, and death of any cause.

**Statistical Analysis**

Baseline lipid values were the average of values at weeks –2 and 0. Final lipid values were those assessed closest to the date of the final angiogram. For patients with final angiography before 2.5 years because of a clinical event, measurements at week 54 were substituted.

To compare baseline characteristics between HDL-C categories, 1-way ANOVA (for continuous variables) or the χ² test (for categorical variables) was used. If the assumptions underlying these tests were not satisfied, Mann–Whitney rank-sum test and Fisher’s exact test, respectively, were used.

To determine whether there was a differential impact of treatment in the 2 HDL-C categories, the relation of fluvastatin patients to placebo patients in the low–HDL-C category was compared with the relation of fluvastatin to placebo in the higher–HDL-C category for both baseline and posttreatment characteristics. This potential treatment group–by–HDL-C category interaction was analyzed using ANOVA for continuous outcome variables (except MLD and percent diameter stenosis) and logistic regression for categorical outcome variables. Multinomial logistic regression analysis was used to compare the distribution of patients categorized as progressors (MLD decrease ≥0.4 mm in any qualifying lesion), regressors (MLD increase ≥0.4 mm in any qualifying lesion and no MLD decrease ≥0.4 mm), and stable (no MLD change ≥0.4 mm in any qualifying lesion). Hierarchical mixed-model regression analysis of MLD and percent diameter stenosis was performed on a per-lesion basis to account for the variability of lesions within patients. The log-rank test was used to analyze time to first clinical event.

MLD and percent diameter stenosis are reported as least square mean±SE. All other variables are reported as mean±SD. All tests of significance were 2-sided with an overall P≤0.05 indicating statistical significance. The Bonferroni procedure was applied to control the error rate associated with the number of tests for a given set of variables. All calculations were performed with Stata (Stata Corporation) or the Statistical Analysis System (SAS Institute).

**Results**

The primary results of LCAS have been published previously. Of the 429 patients randomized, 339 had extensive lipoprotein and coagulation profiles at >1 time point during the trial and evaluable baseline and follow-up angiography. Lipoprotein and coagulation values at week 54 were substituted for week 130 values in 11 patients because final angiography was performed before 2.5 years (because of a clinical event).

**Comparison of Patients with Low Versus Higher Baseline HDL-C**

**Baseline Characteristics**

One fifth of patients (n=68) had HDL-C <0.91 mmol/L (35 mg/dL) (mean 0.82±0.06 mmol/L [31.7±2.2 mg/dL]), versus mean 1.23±0.29 mmol/L [47.4±11.2 mg/dL] in the 271 patients with HDL-C ≥0.91 mmol/L). In a comparison of baseline characteristics (Table 1), low–HDL-C patients were significantly more likely to be male and had significantly increased body-mass index, triglyceride levels (2.18±0.65 mmol/L [193.5±58.0 mg/dL] versus 1.71±0.61 mmol/L [151.7±53.9 mg/dL]; P<0.001), and apo B-100/apo A-I ratio (1.30±0.23 versus 1.00±0.24; P<0.001); they also had significantly decreased total cholesterol (5.50±0.55 mmol/L [212.8±21.2 mg/dL] versus 5.77±0.64 mmol/L [223.3±24.6 mg/dL]; P=0.01), apo A-I (106.9±10.6 mg/dL versus 139.9±28.0 mg/dL; P<0.001), and lipoproteins containing only apo A-I (37.6±6.1 mg/dL versus 47.6±11.9 mg/dL; P<0.001). In addition, they were somewhat more likely (nonsignificant) to smoke and to have prior MI, increased apo C-III in apo B–containing particles (14.8±5.5 mg/dL versus 23.3±12.8 mg/dL), and decreased apo C-III in non–apo B–containing particles (14.8±9.4 mg/dL versus 18.0±8.7 mg/dL). Blood pressure (Table 1), coagulation factors, and diet (not shown) were not different between HDL-C categories.

**Quantitative Coronary Angiography and Clinical Events**

To examine the influence of baseline HDL-C on CAD progression, MLD change was compared in placebo-only patients (ie, excluding patients assigned to receive adjunctive cholesterolamine) in each HDL-C category (Figure 1). Placebo-only patients with low HDL-C (n=21) had significantly more progression than placebo-only patients with higher baseline HDL-C (n=111): MLD decreased 0.250±0.047 mm versus 0.083±0.020 mm (P=0.001).

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**Table 1: Baseline Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low HDL-C (&lt;0.91 mmol/L)</th>
<th>High HDL-C (≥0.91 mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index</td>
<td>30.0 ± 4.0</td>
<td>28.5 ± 3.5</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>1.9 ± 0.4</td>
<td>1.4 ± 0.3</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>5.7 ± 0.9</td>
<td>5.3 ± 0.8</td>
</tr>
<tr>
<td>HDL-C</td>
<td>0.9 ± 0.2</td>
<td>1.2 ± 0.3</td>
</tr>
<tr>
<td>Apo B-100/apo A-I</td>
<td>1.3 ± 0.2</td>
<td>1.1 ± 0.1</td>
</tr>
</tbody>
</table>

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**Table 2: Clinical Events**

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Low HDL-C (&lt;0.91 mmol/L)</th>
<th>High HDL-C (≥0.91 mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>10/68</td>
<td>5/271</td>
</tr>
<tr>
<td>Stable</td>
<td>40/68</td>
<td>322/271</td>
</tr>
</tbody>
</table>
Among all patients, time to first clinical event was not significantly different between low–HDL-C patients (10 of 68 patients with events) and higher–HDL-C patients (33 of 271).

Effect of Fluvastatin in Patients with Low Versus Higher Baseline HDL-C

Baseline Characteristics
After confirmation that patients with low HDL-C had the greatest CAD progression, we examined the effects of fluvastatin in low–HDL-C patients compared with higher–HDL-C patients. Within each HDL-C category, baseline characteristics were comparable between treatment groups except for men ($P$, 0.002) and glucose ($P$, 0.04) (Table 2).

Quantitative Coronary Angiography
Among low–HDL-C patients, fluvastatin significantly reduced CAD progression measured by MLD decrease: $0.065\pm0.036$ mm versus $0.274\pm0.045$ mm with placebo ($P$, 0.0004); respective MLD decreases among higher–HDL-C patients were $0.036\pm0.021$ mm versus $0.083\pm0.019$ mm ($P$, 0.09) (Figure 2). The treatment effect of fluvastatin on MLD change, calculated as the difference between MLD change in fluvastatin and placebo patients, was significantly greater among low–HDL-C patients than among higher–HDL-C patients ($P$, 0.01).

Increase in percent diameter stenosis was also significantly reduced with fluvastatin among low–HDL-C patients: $1.4\pm1.2$% versus $8.4\pm1.6$% with placebo ($P$, 0.01). The treatment effect of fluvastatin on change in percent diameter stenosis was significantly greater in low–HDL-C patients ($P$, 0.01). In both HDL-C categories, fluvastatin significantly improved the categorization of patients as progressors, regressors, or stable (Table 3), with low–HDL-C placebo patients having the highest frequency of progression (60%).

Sex, age, and glucose were assessed as potential influences on the relation of MLD change to treatment, HDL-C category, and the treatment–by–HDL-C interaction. Only sex had a significant effect ($P$, 0.05), but because no placebo-treated women had low HDL-C, the 3-way interaction of sex by treatment by HDL-C category could not be evaluated. The 2-way interactions of sex by treatment and sex by HDL-C category were not significant.

Lipids
The effects of fluvastatin on lipids and apolipoproteins were similar in patients with low or higher HDL-C (Table 3). A comparison of baseline and final values showed that the major effect of fluvastatin in both HDL-C categories was to lower LDL-C and apo B-100: respective reductions with fluvastatin were 24.6% and 11.6% in low–HDL-C patients.
The difference between change in MLD in fluvastatin and placebo low–HDL-C patients was significantly greater than in higher–HDL-C patients as assessed by the interaction of treatment and HDL-C category.

**Clinical Events**

Event-free survival was significantly improved with fluvastatin in low–HDL-C patients ($P=0.002$), with events in 2 of 43 fluvastatin and 8 of 25 placebo patients (Figure 3). Event-free survival did not differ among higher–HDL-C patients; 19 of 128 fluvastatin and 14 of 143 placebo patients had events.

**Discussion**

In LCAS, which studied patients with mildly to moderately elevated LDL-C, patients who also had low HDL-C at baseline had more CAD progression than patients with higher HDL-C.

Low–HDL-C patients had increased triglyceride levels and body-mass index values and were almost exclusively male. Consistent with having low HDL-C, they also had reduced apo A-I and lipoprotein A-I. Although total cholesterol was also lower in these patients, LDL-C and apo B-100 were similar, with a more unfavorable apo B-100/apo A-I ratio. Although not statistically significant, low–HDL-C patients tended to have a higher incidence of cigarette smoking, increased plasma glucose and apo C-III in apo B–containing particles, and decreased apo C-III in non–apo B–containing particles, which may be a marker for delayed clearance of triglyceride-rich lipoproteins. Low HDL-C is associated with the metabolic syndrome consisting of impaired glucose metabolism; postprandial lipemia; small, dense LDL; and LDL that is more susceptible to oxidation. Because of the clustering of risk factors, low HDL-C may be a marker rather than a mechanism for increased progression. Using methods such as ultracentrifugation to measure LDL and VLDL,

**Figure 2.** Among low–HDL-C patients, fluvastatin patients had significantly less CAD progression measured by MLD change (mean±SE). The difference between change in MLD in fluvastatin and placebo low–HDL-C patients was significantly greater than in higher–HDL-C patients as assessed by the interaction of treatment and HDL-C category.
several studies have identified high-risk subgroups that may benefit the most from therapy. Despite the different methods used, the high-risk group had lower HDL-C in all cases.

Unlike methods such as ultracentrifugation and apolipoprotein measurement, which are not routinely used, HDL-C is routinely measured and therefore may frequently play a role in decisions regarding risk assessment.

### Table 3: Treatment Effects at Final Follow-up

<table>
<thead>
<tr>
<th>Final Parameter</th>
<th>HDL-C &lt;35 mg/dL</th>
<th>HDL-C &gt;=35 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>FL (n=43)*</td>
<td>PL (n=25)*</td>
</tr>
<tr>
<td>LDL-C</td>
<td>181.2±27.90</td>
<td>210.2±25.32</td>
</tr>
<tr>
<td>HDL-C</td>
<td>37.1±4.56</td>
<td>34.0±4.57</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>185.6±69.71</td>
<td>194.6±89.40</td>
</tr>
<tr>
<td>LpA-I</td>
<td>41.6±6.84</td>
<td>37.1±8.64</td>
</tr>
<tr>
<td>Apo A-I</td>
<td>116.3±15.91</td>
<td>106.4±13.52</td>
</tr>
<tr>
<td>Apo B-100</td>
<td>121.3±21.37</td>
<td>142.1±20.44</td>
</tr>
<tr>
<td>Apo B-100/apo A-I</td>
<td>1.06±0.239</td>
<td>1.35±0.224</td>
</tr>
<tr>
<td>Apo C-III: B</td>
<td>21.2±12.64</td>
<td>22.9±12.71</td>
</tr>
<tr>
<td>Apo C-III: nonB</td>
<td>14.6±6.22</td>
<td>14.0±5.11</td>
</tr>
</tbody>
</table>

Categorical CAD change,† n (%)

| Progressor       | 16 (37.2) | 15 (60.0) | 38 (29.7) | 58 (40.6) |
| Regressor         | 6 (14.0)  | 1 (4.0)   | 19 (14.8) | 13 (9.1)  |
| Stable            | 21 (48.8) | 9 (36.0)  | 71 (55.5) | 72 (50.3) |

Final parameter values are mg/dL (mean±SD) except where noted.
Abbreviations as in Table 2.
P=0.004, progressors versus regressors; P=0.01, progressors versus stable.
*Percent change values include only patients with both baseline and final values, ranging from n=295 (for apo C-III: B) to n=336 (for lipids).
†Fluvastatin versus placebo in both HDL-C categories.

**Figure 3.** Time to first clinical event (PTCA, CABG, definite or probable MI, unstable angina requiring hospitalization, or death of any cause) in patients with low HDL-C (top) and higher HDL-C (bottom). Among low–HDL-C patients, fluvastatin patients had significantly improved event-free survival, but there was no difference with treatment among higher–HDL-C patients.
and treatment. The increased CAD progression seen in low–HDL-C patients is consistent with numerous studies that have shown that these patients are at increased risk for CAD events. Yet despite their known risk for CAD events, low–HDL-C patients in LCAS were less frequently treated with a statin before the study (14.7% versus 20.3%), perhaps reflecting confusion as to whether the treatment of low–HDL-C patients should focus on raising HDL-C or lowering LDL-C.

The treatment effect of fluvastatin on MLD change, calculated as the difference between MLD change in fluvastatin patients and placebo patients, was significantly greater among low–HDL-C patients than higher–HDL-C patients \( (P=0.01) \). Event-free survival was also significantly improved with fluvastatin in low–HDL-C but not higher–HDL-C patients. As would be expected with a statin, the primary impact of fluvastatin was to lower LDL-C and apo B-100. Significant but more modest changes were seen in HDL-C, apo A-I, and triglyceride, and no significant changes were seen in Lp(a), apo C-III in apo B–containing lipoproteins, apo C-III in non-apo B-containing lipoproteins, fibrinogen, and factor VIII-c compared with placebo.

The results from LCAS showing the greatest angiographic and clinical benefit with treatment in low–HDL-C patients are in contrast to an earlier trial of cholestyramine monotherapy. In the Lipid Research Clinics Coronary Primary Prevention Trial, patients with HDL-C \( \geq 1.29 \) mmol/L (50 mg/dL) had the greatest benefit on CAD death or MI, whereas patients with HDL-C <1.03 mmol/L (40 mg/dL) had no benefit (adjusted incidence ratios of 0.75 versus 1.13). However, increased benefit in lower–HDL-C patients has been reported in statin trials with clinical events as the primary endpoint (Figure 4). In the Scandinavian Simvastatin Survival Study (4S), West of Scotland Coronary Prevention Study (WOSCOPS), and Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS), statin therapy reduced the risk for coronary events in lower–HDL-C patients to approximately that of placebo patients. As would be expected with a statin, the primary impact of fluvastatin was to lower LDL-C and apo B-100. Fluvastatin, like all statins, reduces not only LDL but also IDL and VLDL remnant particles (thought to be atherogenic). These triglyceride-rich particles are frequently increased in low–HDL-C patients. Because HDL plays a role in reverse cholesterol transport, may prevent LDL oxidation, and may have direct protective effects on the vessel wall, the atherogenic effects of LDL-C and apo B-100–containing lipoproteins may have been more pronounced in low–HDL-C patients and thus reductions in LDL-C with fluvastatin gave greater benefit. In addition, HDL-C was also significantly improved. Unfortunately, one of the limita-

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**TABLE 4. Summary of Angiographic Trials Discussed**

<table>
<thead>
<tr>
<th>Trial</th>
<th>n*</th>
<th>LDL-C</th>
<th>HDL-C</th>
<th>Drug Therapy (assigned dosage/d)</th>
<th>%Δ From Baseline†</th>
<th>Baseline MLD† (mm)</th>
<th>ΔMLD (mm)</th>
<th>ΔStenosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCAS</td>
<td>339</td>
<td>146</td>
<td>43</td>
<td>Fluvastatin 40 mg (+cholestryamine 4–12 g)</td>
<td>-25</td>
<td>1.64</td>
<td>0.07</td>
<td>2.2</td>
</tr>
<tr>
<td>LCAS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HDL-C &lt;35 mg/dL</td>
<td>68</td>
<td>143</td>
<td>32</td>
<td>Fluvastatin 40 mg (+cholestryamine 4–12 g)</td>
<td>-25</td>
<td>1.67</td>
<td>0.21</td>
</tr>
<tr>
<td>BECAIT</td>
<td>81</td>
<td>180</td>
<td>34</td>
<td>Bezafibrate 600 mg</td>
<td>-3.5</td>
<td>1.82</td>
<td>0.11</td>
<td>2.6</td>
</tr>
<tr>
<td>LOCAT†‡</td>
<td>372</td>
<td>138</td>
<td>31</td>
<td>Gemfibrozil 1200 mg</td>
<td>-4.5</td>
<td>1.59</td>
<td>0.04</td>
<td>0.9</td>
</tr>
</tbody>
</table>

†Mean (median in BECAIT) in drug-treated group.
‡Angiographic analysis of primary segments, comprising graft-dependent segments and native coronary segments unaffected by bypass grafts.

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**Figure 4.** Statin therapy in lower–HDL-C patients reduces coronary risk to approximately that of higher–HDL-C patients on placebo. 4S indicates Scandinavian Simvastatin Survival Study (highest and lowest quartiles); WOSCOPS, West of Scotland Coronary Prevention Study (at or above the median versus below the median); AFCAPS/TexCAPS, Air Force/Texas Coronary Atherosclerosis Prevention Study (highest and lowest tertiles).
tions of this study was the lack of women with low HDL-C; consequently, we were unable to examine the potential influence of sex on the treatment effect of fluvastatin in low–HDL-C patients.

Two recent angiographic trials have examined the effects of fibrate therapy on CAD progression in low–HDL-C patients (Table 4). In the Bezafibrate Coronary Atherosclerosis Intervention Trial,21 median MLD decrease was 0.06 mm with bezafibrate and 0.17 mm with placebo; estimation of a treatment effect on the basis of this difference indicated 0.13 mm less progression with bezafibrate ($P=0.049$). In the Lopid Coronary Angiography Trial,22 gemfibrozil patients had significantly less CAD progression as measured by MLD decrease in all native coronary segments, 0.04 mm versus 0.09 mm in placebo patients. A comparison of these studies with LCAS (Table 4) suggests that statin therapy is at least as beneficial as fibrate therapy in low–HDL-C patients. In addition, the safety, effectiveness, and morbidity and mortality benefits of statins have been clearly documented in numerous clinical trials, whereas the data on fibrates remain incomplete.

The combined results of the statin and fibrate trials raise the question of whether combination therapy to lower LDL-C and raise HDL-C might provide greater benefit. Several studies have shown that combinations of a statin plus either nicotinic acid23 or gemfibrozil24 provide additional benefits of reduced triglyceride levels, increased HDL-C, and improved LDL particle size; combination therapy has been shown to produce greater angiographic benefit than monotherapy.25 Adding low-dose nicotinic acid (1 to 2 g/d) to a statin is particularly appealing because of the low cost and additional benefit of reducing Lp(a).26 Future studies should address the question of whether a statin in conjunction with an agent to increase HDL-C, such as nicotinic acid or a fibrate, produces greater clinical benefit than a statin alone.

In the NCEP guidelines, the primary focus of therapy is reduction of LDL-C, to ≤2.59 mmol/L (100 mg/dL) in CAD patients. In CAD patients with low HDL-C who require drug therapy to reduce elevated LDL-C, the drug selected should increase HDL-C as well as lower LDL-C. The guidelines also provide for the consideration of nicotinic acid in CAD patients with low HDL-C even if LDL-C is below the initiation level for drug therapy.

Our findings support the NCEP guidelines: the first goal of treatment should be to lower LDL-C, even in patients whose LDL-C is only mildly to moderately elevated. Although low–HDL-C patients in LCAS had more CAD progression than patients with normal or elevated HDL-C, low–HDL-C patients also had the greatest angiographic benefit with fluvastatin treatment, even though the predominant lipid-regulating effect of fluvastatin is to lower LDL-C. In summary, statin therapy provides substantial benefits to patients with CAD, low HDL-C, and mild to moderate elevations of LDL-C.

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References


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