Incidence of New Atherothrombotic Brain Infarction in Older Persons With Prior Myocardial Infarction and Serum Low-Density Lipoprotein Cholesterol ≥125 mg/dl Treated With Statins Versus No Lipid-Lowering Drug

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Background. We report the incidence of new atherothrombotic brain infarction (ABI) in older men and women with prior myocardial infarction and a serum low-density lipoprotein (LDL) cholesterol of ≥125 mg/dl treated with statins and with no lipid-lowering drug.

Methods. The incidence of new ABI was investigated in an observational prospective study of 1410 men and women, mean age 81 ± 9 years, with prior myocardial infarction and a serum LDL cholesterol of ≥125 mg/dl treated with statins (679 persons or 48%) and with no lipid-lowering drug (731 persons or 52%). Follow-up was 36 ± 21 months.

Results. At follow-up, the stepwise Cox regression model showed that significant independent predictors of new ABI were age (risk ratio = 1.04 for a 1-year increase in age), cigarette smoking (risk ratio = 3.5), hypertension (risk ratio = 3.1), diabetes mellitus (risk ratio = 2.3), initial serum LDL cholesterol (risk ratio = 1.04 for each 1 mg/dl increase), initial serum high-density lipoprotein cholesterol (risk ratio = 0.97 for each 1 mg/dl increase), prior stroke (risk ratio = 2.5), and use of statins (risk ratio = 0.40). The Cochran-Armitage test showed a trend in the reduction of new ABI in persons treated with statins as the level of serum LDL cholesterol decreased (p < .0001).

Conclusions. Use of statins caused a 60%, significant, independent reduction in new ABI in older men and women with prior myocardial infarction and a serum LDL cholesterol of ≥125 mg/dl.
679 persons treated with a statin, 603 (89%) were treated with simvastatin, 68 (10%) were treated with pravastatin, and eight (1%) were treated with lovastatin. The attitude of different physicians toward treating hypercholesterolemia in older persons with prior myocardial infarction determined whether or not statins were prescribed. Follow-up was 36 ± 21 months (range 1 to 133 months).

Chi-square tests were used to analyze dichotomous variables, and Student’s t tests were used for continuous variables (Tables 1, 2, and 4). Table 3 shows the prognostic variables for new ABI and their regression coefficients in the stepwise Cox regression model. The Cochran-Armitage test was used to examine if there was a trend in the reduction of new ABI in persons treated with statins as the last level of serum LDL cholesterol decreased (Table 5).

**RESULTS**

Table 1 shows the baseline characteristics of the persons treated with statins versus no lipid-lowering drug and lists levels of statistical significance. In persons treated with statins, the initial serum LDL cholesterol was 152 ± 26 mg/dl and the last serum LDL cholesterol was 98 ± 17 mg/dl (p < .0001); the initial serum HDL cholesterol was 40 ± 9 mg/dl and the last serum HDL cholesterol was 44 ± 10 mg/dl (p < .0001); and the initial serum triglycerides level was 123 ± 51 mg/dl and the last serum triglycerides level was 108 ± 45 mg/dl (p < .0001). In persons treated with no lipid-lowering drug, the initial serum LDL cholesterol was 155 ± 23 mg/dl and the last serum LDL cholesterol was 156 ± 23 mg/dl (p not significant); the initial serum HDL cholesterol was 39 ± 9 mg/dl and the last serum HDL cholesterol was 39 ± 8 mg/dl (p not significant); and the initial serum triglycerides level was 123 ± 53 mg/dl and the last serum triglycerides level was 124 ± 51 mg/dl (p not significant).

Table 2 shows the incidence of new ABI in persons treated with statins versus no lipid-lowering drug for the age groups of 60 to 70 years, 71 to 80 years, 81 to 90 years, and 91 to 100 years and lists levels of statistical significance. Table 5 shows the incidence of new ABI in persons treated with statins with the last serum LDL cholesterol levels of <90 mg/dl, 90 to 99 mg/dl, 100 to 110 mg/dl, 111 to 120 mg/dl, 121 to 130 mg/dl, and >130 mg/dl.

**DISCUSSION**

In the Scandinavian Simvastatin Survival Study, persons with coronary artery disease (CAD) and hypercholesterolemia, the initial serum LDL cholesterol was 155 ± 23 mg/dl and the last serum LDL cholesterol was 98 ± 17 mg/dl (p < .0001); the initial serum HDL cholesterol was 40 ± 9 mg/dl and the last serum HDL cholesterol was 44 ± 10 mg/dl (p < .0001); and the initial serum triglycerides level was 123 ± 51 mg/dl and the last serum triglycerides level was 108 ± 45 mg/dl (p < .0001). In persons treated with no lipid-lowering drug, the initial serum LDL cholesterol was 156 ± 23 mg/dl and the last serum LDL cholesterol was 156 ± 23 mg/dl (p not significant); the initial serum HDL cholesterol was 39 ± 9 mg/dl and the last serum HDL cholesterol was 39 ± 8 mg/dl (p not significant); and the initial serum triglycerides level was 123 ± 53 mg/dl and the last serum triglycerides level was 124 ± 51 mg/dl (p not significant).

Table 2 shows the incidence of new ABI in persons treated with statins versus no lipid-lowering drug and lists the level of statistical significance. Table 3 shows the prognostic variables for new ABI and their regression coefficients in the stepwise Cox regression model. Table 4 shows the incidence of new ABI in persons treated with statins versus no lipid-lowering drug for the age groups of 60 to 70 years, 71 to 80 years, 81 to 90 years, and 91 to 100 years and lists levels of statistical significance.
EFFECT OF STATINS ON STROKE

Table 5. Incidence of New Atherothrombotic Brain Infarction in Older Persons Treated With Statins for Ranges of Last Serum Low-Density Lipoprotein Cholesterol Levels

<table>
<thead>
<tr>
<th>Last Low-Density Lipoprotein Cholesterol</th>
<th>New Atherothrombotic Brain Infarction, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;90 mg/dl</td>
<td>16/225 (7)</td>
</tr>
<tr>
<td>90 to 99 mg/dl</td>
<td>38/231 (16)</td>
</tr>
<tr>
<td>100 to 110 mg/dl</td>
<td>11/103 (11)</td>
</tr>
<tr>
<td>111 to 120 mg/dl</td>
<td>16/52 (31)</td>
</tr>
<tr>
<td>121 to 130 mg/dl</td>
<td>8/35 (23)</td>
</tr>
<tr>
<td>&gt;130 mg/dl</td>
<td>9/33 (27)</td>
</tr>
</tbody>
</table>

Note: The Cochran-Armitage test showed a trend in the reduction of new atherothrombotic brain infarction as the last level of serum low-density lipoprotein cholesterol decreased (p < .0001).

...olemia treated with simvastatin had at 5.4-year median follow-up a 30% significant reduction in new stroke (1). In the Cholesterol and Recurrent Events Trial, persons aged 65 to 75 years with myocardial infarction, a serum LDL cholesterol ≥115 mg/dl, and a serum total cholesterol <240 mg/dl treated with pravastatin had at 5-year median follow-up a 40% significant reduction in new stroke (2). In the Long-Term Intervention With Pravastatin in Ischaemic Disease Study, persons with myocardial infarction or unstable angina pectoris and a mean serum total cholesterol of 218 mg/dl had at 6.1-year mean follow-up a 19% significant reduction in new stroke (3).

In the present study of 1410 persons, mean age 81 years, persons with prior myocardial infarction and a serum LDL cholesterol ≥125 mg/dl had at 36-month follow-up a 14% incidence of new ABI if they were treated with statins and a 26% incidence of new ABI if they were treated with no lipid-lowering drug. The significant reduction in new ABI in persons treated with statins occurred in persons aged 60 to 70 years, 71 to 80 years, and 81 to 90 years, but not in persons older than 90 years.

Significant independent risk factors for new ABI in this study were age (risk ratio = 1.04 for a 1-year increase in age), cigarette smoking (risk ratio = 3.5), systemic hypertension (risk ratio = 3.1), diabetes mellitus (risk ratio = 2.3), initial serum LDL cholesterol (risk ratio = 1.01 for each 1 mg/dl increase), initial serum high-density lipoprotein cholesterol (risk ratio = 0.97 for each 1 mg/dl increase), prior stroke (risk ratio = 2.5), and use of statins (risk ratio = 0.40). The Cochran-Armitage test showed a trend in the reduction of new ABI in persons treated with statins as the level of serum LDL cholesterol decreased (p < .0001).

Acknowledgment

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References


Received October 30, 2001
Accepted December 3, 2001