The relationship between lipids and stroke is complex. In most epidemiological cohorts, there is a direct relationship between cholesterol levels and ischemic stroke. The relationship of lipids to ischemic stroke, however, varies by stroke subtype, with associations strongest for atherosclerotic subtypes. Conversely, there is an increased risk of intracerebral hemorrhage (ICH) at low cholesterol levels, and there is evidence that small vessel disease may share a similar profile of inverse association with lipid levels. The associations also depend on the specific lipid component considered, with the data strongest for total cholesterol (TC) and low-density lipoprotein-cholesterol (LDL-C). Given the availability of increasingly potent lipid-lowering agents, understanding the relationship between dyslipidemia and stroke may improve primary and secondary stroke prevention strategies.

Here, we review the literature on the relationship between dyslipidemia and stroke, with a focus on lipid screening recommendations and evidence-based approaches to management.

**Lipid Parameters and Stroke Risk**

**Total and LDL-C**

In most, but not all, observational studies, there is an association between higher total and LDL-C levels and increased ischemic stroke risk (Table 1).1–12

In addition, most observational studies also found an association between lower TC and LDL-C levels and increased risk of hemorrhagic stroke (Table 2).2,13–17 A recent meta-analysis of 23 studies showed an inverse dose–response association between TC and hemorrhagic stroke (odds ratio [OR], 0.85 per 1 mmol/L increment; 95% confidence interval [95% CI], 0.80–0.91).18 The mechanism of this association remains unclear. Some studies, however, have shown low serum LDL-C levels in patients with liver disease19 and hematologic malignancies20 who are at a higher risk of ICH. This hypothesis can be tested in large population-based cohorts.

Overall, epidemiological studies suggest competing stroke risk related to TC levels in the general population; high TC is associated with higher risk of ischemic stroke, whereas lower levels are associated with higher risk of brain hemorrhage.

Present data do not permit specification of an acceptable cholesterol threshold with regard to these competing risks in either men or women, however.

**High-Density Lipoprotein-Cholesterol and High-Density Lipoprotein Subfractions**

In some studies, there is an inverse relationship between high-density lipoprotein-cholesterol (HDL-C) and stroke (Table 1).5,7,8 A systematic review of 10 prospective studies found a decreased risk of ischemic stroke ranging from 11% to 15% for each 10-mg/dL increase in HDL-C.21

Because studies of the association between HDL-C and stroke yielded mixed results, and recent evidence showed no benefit of HDL-increasing medications on ischemic stroke risk,22 some suggest that the relationship between HDL and cerebrovascular disease is a function of HDL-C subfractions rather than of total HDL-C. HDL has 2 main subfractions: larger and less dense HDL-C (HDL2) and smaller and denser HDL-C (HDL3). These subfractions differ in their biological activity, biochemical properties, and vascular metabolism.

HDL3, more so than HDL2, seems to inhibit LDL oxidation and protect against atherosclerosis by its action on the vascular endothelium.

In the Northern Manhattan Study (NOMAS), HDL subfractions had differential effects on the risk of carotid disease; there was a direct relationship between HDL2 and plaque thickness and an inverse relationship between HDL3 and plaque area.23 In a nested prospective case–control analysis from the Circulatory Risk in Community Study, small- and medium-sized HDL particles were associated with reduced risk of ischemic stroke, in particular, lacunar infarcts, and ICH, whereas HDL2 was not associated with stroke risk.24 More studies are needed to better understand the relationship of HDL subfractions and stroke risk.

**Triglycerides**

Epidemiological studies evaluating triglycerides and ischemic stroke also show mixed results, partly because of differential use of both fasting and nonfasting levels (Table 1).5,11,12 In...
addition, in a meta-analysis of 64 studies, there was an association between higher triglyceride levels and relative risk (RR) of stroke (adjusted RR, 1.05; 95% CI, 1.03 to 1.07) for each 10-mg/dL increase in baseline triglycerides; fasting and nonfasting status were not specified. Studies have also shown that triglycerides levels are inversely associated with hemorrhagic stroke risk. Lipoprotein(a)

Lipoprotein(a) (Lp(a)) has been identified as an emerging risk factor for cardiovascular disease. Plasma levels of Lp(a) are influenced by genetic factors, with substantial differences across ethnic groups, with levels being highest among blacks. Studies on the relationship between Lp(a) and risk of ischemic stroke yielded mixed results. In a nested case-control study of 15,000 healthy predominantly white middle-aged physicians, Lp(a) levels were not associated with stroke risk. In a European cohort, plasma Lp(a) levels also were not associated with ischemic stroke. In Atherosclerosis Risk in Communities, Lp(a) levels ≥30 mg/mL were associated with increased risk of ischemic stroke in black and white women, but not in white men. In a NOMAS case-control study,

<table>
<thead>
<tr>
<th>Lipid Profile Component</th>
<th>Study</th>
<th>Characteristics</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>Alpha-Tocopherol, Beta Carotene Cancer Prevention Study</td>
<td>28,000 men smokers</td>
<td>Increased risk of ischemic stroke with a total cholesterol levels ≥7 mmol/L (≥271 mg/dL; HR, 1.25; 95% CI, 0.99–1.57)</td>
</tr>
<tr>
<td></td>
<td>Asia Pacific Cohort Studies Collaboration</td>
<td>352,033 individuals from Asia and New Zealand</td>
<td>For every 1-mmol/L increase in total cholesterol, there was a 25% (95% CI, 13–40) increase in ischemic stroke rate</td>
</tr>
<tr>
<td></td>
<td>Women's Health Study</td>
<td>Prospective cohort study of 27,937 US women aged ≥45 y</td>
<td>Total cholesterol level was associated with ischemic stroke (adjusted HR per 1-mmol/L increase for ischemic stroke of 1.17 (95% CI, 1.06–1.30)</td>
</tr>
<tr>
<td></td>
<td>Eurostroke Project</td>
<td>22,183 subjects</td>
<td>No relationship between total cholesterol level and ischemic stroke</td>
</tr>
<tr>
<td></td>
<td>Women's Pooling Project</td>
<td>24,343 US women &lt;55 y of age with no previous cardiovascular disease</td>
<td>Higher total cholesterol was associated with increased risk of ischemic stroke (HR, 1.69; 95% CI, 0.91–3.13, for topmost quintile compared with the lower-most one)</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>Women's Health Study</td>
<td>Prospective cohort study of 27,937 US women aged ≥45 y</td>
<td>Serum LDL cholesterol was associated with increased risk of ischemic stroke (HR, 1.74; 95% CI, 1.14–2.66; ( P_{\text{trend across quintiles}}=0.003 ))</td>
</tr>
<tr>
<td></td>
<td>The Atherosclerosis Risk in Communities</td>
<td>14,175 middle-aged men and women without clinical cardiovascular disease</td>
<td>Nonsignificant association between LDL cholesterol and ischemic stroke (HR, 1.26; 95% CI, 0.91–1.76, for topmost quintile compared with the lower-most one)</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>Copenhagen City Heart Study</td>
<td>19,696 women and men at least 20 y old</td>
<td>47% reduction in the risk of nonhemorrhagic stroke for every 1-mmol/L increase in HDL</td>
</tr>
<tr>
<td></td>
<td>Northern Manhattan Stroke Study</td>
<td>539 patients and 905 controls</td>
<td>Inverse relationship between ischemic stroke and HDL level ≥35 mg/dL (0.91 mmol/L; OR, 0.53; 95% CI, 0.39–0.72)</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular Health Study</td>
<td>5,201 adults aged ≥65 living in US communities, plus a recruitment of 687 blacks 3 y later</td>
<td>Higher HDL cholesterol level was associated with a decreased risk of ischemic stroke in men, but not in women</td>
</tr>
<tr>
<td></td>
<td>The Atherosclerosis Risk in Communities</td>
<td>14,175 middle-aged men and women without clinical cardiovascular disease</td>
<td>No relationship between HDL cholesterol and ischemic stroke in men and a nonsignificant association in women</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>The Atherosclerosis Risk in Communities</td>
<td>14,175 middle-aged men and women without clinical cardiovascular disease</td>
<td>Fasting triglyceride levels were not associated with ischemic stroke</td>
</tr>
<tr>
<td></td>
<td>Physicians' Health Study</td>
<td>Men, 296 strokes and 296 controls</td>
<td>No association between triglyceride level and ischemic stroke</td>
</tr>
<tr>
<td></td>
<td>Copenhagen City Heart Study</td>
<td>Prospective, population-based cohort study comprising ≈14,000 patients</td>
<td>15% (95% CI, 9–22) increased risk of ischemic stroke for each 89-mg/dL increase in nonfasting triglycerides</td>
</tr>
<tr>
<td></td>
<td>Women's Health Study</td>
<td>Prospective cohort study of 27,937 US women aged ≥45 y</td>
<td>The highest tertile of nonfasting but not fasting triglyceride level was associated with increased ischemic stroke risk when compared with lowest tertile</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; HDL, high-density lipoprotein; HR, hazard ratio; and LDL, low-density lipoprotein.
Lp(a) levels ≥30 mg/dL at baseline were associated with an increased risk of ischemic stroke. This association was more pronounced among men and blacks.30 The effects of Lp(a), therefore, may depend on race-ethnic and other demographic factors, but more research is needed.

Lipids and Ischemic Stroke Subtypes
Some of the discrepant results among observational studies of lipids and stroke risk may be explained by the differential association with ischemic stroke subtypes: there is a stronger association between lipids and strokes because of large artery atherosclerosis. In a case–control study, the association between cholesterol and ischemic stroke risk was strongest for large artery atherosclerosis (OR, 3.2).31 The association between dyslipidemia and large artery atherosclerotic stroke subtype was also shown in other studies.32,33

On the contrary, not all studies showed an association between dyslipidemia and lacunar stroke. In case–control studies, there have been associations between levels of TC31 and LDL34 with lacunar stroke. Other studies, however, did not show an association between dyslipidemia and lacunar stroke.32,33 Thus, the relationship between dyslipidemia and lacunar stroke is complex and likely influenced by genetic and demographic factors in different patient populations, as well as differences in defining stroke subtypes.

Although dyslipidemia is a risk factor for coronary heart disease, most studies showed no association between dyslipidemia and embolic stroke.31–33

**Lipids, White Matter Disease, and Cerebral Microbleeds**
White matter hyperintensity (WMH), or leukoaraiosis, has been associated with stroke risk factors including age, hypertension, and smoking.33 Because WMH, cerebral microbleeds, and deep ICHs are often considered different manifestations of small vessel disease, the relationship between lipids and each of WMH and cerebral microbleeds may help explain the relationship of lipids to small vessel disease. In fact, studies have shown an inverse relationship between dyslipidemia and both WMH36,37 and cerebral microbleeds,38 providing evidence that lower lipid levels may impair small vessel structure or function.

Taken together, the above data provide some evidence of the inverse association between small vessel disease (WMH and CMBs) and hyperlipidemia. This may relate to the role that cholesterol plays in the architecture and integrity of the normal endothelium of small vessels; thus, low lipid levels may interfere with the integrity of the endothelium or impair endothelial reparative processes, causing leakage or obstruction of the small vessels. The exact mechanism remains uncertain, and more studies are needed to better characterize the mechanism of this association.

**Screening for Lipid Levels After Stroke**
In patients with ischemic stroke, a serum lipid profile including TC, LDL, HDL, and triglycerides should be performed.39 On the contrary, given the scarcity of evidence, routine testing for other lipid components such as Lp(a) and HDL subfractions is not recommended.

The LDL-C usually reported in the lipid profile is generally calculated using the Friedewald formula40:

\[
LDL - C = TC - (\text{very low - density lipoprotein} - \text{cholesterol} + \text{HDL} - C).
\]

This formula is more accurate in the fasting state, because in nonfasting patients, postprandial chylomicrons may contribute to TC levels and make the measurement less accurate. In addition, this method is inaccurate when the triglyceride level is ≥400 mg/dL and has a higher error margin when the LDL is ≤70 mg/dL.41 Direct assays have been developed to measure cholesterol level. Although direct assays are much more expensive than using the Friedwald formula, they may
be needed to give an accurate LDL level in certain cases, such as when the triglycerides level is ≥400 mg/dL. Most clinical trials and lipid management guidelines were based on the estimated LDL level, however.

The timing of lipid measurements after stroke may be less important than after myocardial infarction. There is evidence that lipid levels after stroke do not decline as markedly as after myocardial infarction.\(^1\) In a meta-analysis of 68 studies that included >300,000 patients, moreover, the association between lipid components and ischemic stroke persisted even when measured in nonfasting patients.\(^4\) As noted above, associations with triglycerides were even more prominent in the nonfasting state. Therefore, although the lipid profile is preferably measured fasting, it can probably be tested even in the nonfasting state,\(^4\) and at any time after the stroke, and should include at least TC, LDL, and HDL-C levels.

**Lipid-Lowering Therapy and Stroke**

**Statin Therapy in Primary Stroke Prevention**

In addition to their cardiovascular benefits, statins have demonstrated efficacy in reducing stroke risk. In primary stroke prevention trials, several statins have been associated with reductions in risk of stroke ranging from 11% to 40%. The Heart Protection Study (HPS) randomized >20,000 patients aged 40 to 80 years with high risk of vascular disease to simvastatin 40 mg daily versus placebo. There was a 25% reduction in stroke risk without an increase in the risk of hemorrhagic stroke.\(^4\) More aggressive treatment was associated with a further reduction in risk. In the Treating to New Targets (TNT) study, compared with atorvastatin 10 mg daily, atorvastatin 80 mg daily was associated with a 25% reduction in stroke risk that correlated with reductions in LDL. Furthermore, meta-analyses of lipid therapy and stroke showed that with each 1-mmol/L reduction in LDL-C, there was ≈20% RR reduction in ischemic stroke.\(^5\)\(^6\)

**Statin Therapy in Secondary Stroke Prevention**

A post hoc analysis of the HPS study showed that in the 3,280 patients with a history of cerebrovascular disease without coronary disease, simvastatin treatment was associated with a 5% reduction in the risk of major cardiovascular events or death when compared with placebo.\(^5\) The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial, however, provides the most direct evidence on the role of statins in secondary stroke prevention. SPARCL randomized 4,731 patients with stroke or transient ischemic attack presumed to be of atherosclerotic origin.\(^\text{36}\) The guidelines do recommend treatment for patients with stroke with LDL levels <100 mg/dL, however, which is even lower than the criteria for inclusion in SPARCL, reflecting both the recognition that patients with stroke have a similar high risk of future cardiovascular events because patients with other forms of atherosclerotic disease and that use of statin therapy should be based on overall risk rather than only on lipid levels.\(^\text{49}\)

SPARCL is the first clinical trial to prove the benefit of high-dose statin therapy in secondary stroke prevention, but the effect was modest with a number needed to treat 50 >5 years. SPARCL had several limitations, however. For instance, patients were randomized at 1 to 6 months after stroke, the period where the risk of stroke recurrence falls, especially in patients with large artery atherosclerosis in whom statins may provide the most stroke prevention benefit. Ongoing trials are addressing the role of statin therapy given immediately after stroke, not only to reduce lipid levels and prevent recurrent stroke but also to ameliorate cerebral injury related to the stroke itself. For example, the Neuroprotection with Statin Therapy for Acute Recovery (NeuSTART) trial is a phase II trial randomizing patients with acute ischemic stroke to lovastatin 640 mg daily for 3 days versus placebo to determine the safety and efficacy ofLovastatin in reducing infarct size and promoting stroke recovery, which may be a function of the pleiotropic effects of statins.\(^\text{50}\) In addition, SPARCL did not establish a target LDL.

**Statins Therapy Beyond Lipid Control**

Investigators suggest that a beneficial pleiotropic effect of statins could be through mechanisms different than action on cholesterol metabolism in the liver. These other potential mechanisms include inhibition of the inflammatory cascade, antioxidant effects, upregulation of nitric oxide synthase with consequent increase in cerebral blood flow, plaque stabilization, and modulating coagulation and platelet function. These mechanisms not only have stroke prevention implications but also contribute to improved functional outcome in acute ischemic stroke.

**Other Lipid-Lowering Drugs in Stroke Prevention**

The benefit of nonstatin lipid-lowering agents for primary or secondary stroke prevention is not as well established. Although niacin increases HDL levels, its benefit in reducing the risk of cerebrovascular events remains uncertain. A meta-analysis of 11 studies (n=9959 subjects) showed no association between the use of niacin and the risk of stroke (OR, 0.88; 95% CI, 0.50 to 1.54).\(^\text{51}\)

Fibric acid derivatives can also be used to lower triglycerides and increase HDL-C levels, but their efficacy in reducing incident stroke is uncertain. The Veterans Affairs-HDL Intervention Trial (VA-HIT) among men with coronary artery disease and low HDL-C, fenofibrate provided a 31% reduction in stroke risk (P=0.036).\(^\text{52}\) A recent meta-analysis, however, included 18 trials, and >45,000 patients provided no evidence that fibrates reduce stroke risk (RR reduction, -3%; 95% CI, -16 to 9).\(^\text{53}\)

Ezetimibe inhibits the intestinal absorption of cholesterol, reducing TC levels. The recently published Improved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) showed that the addition of ezetimibe 10 mg daily to simvastatin 40 mg daily resulted in a
significant reduction in stroke risk (hazard ratio, 0.86; 95% CI, 0.73 to 1.00). A meta-analysis that included 78 trials of lipid-lowering agents showed no significant stroke risk reduction of nonstatin lipid-lowering interventions including fibrates, other treatments, and diet (OR, 0.92; 95% CI, 0.69 to 1.23).15

**Novel Lipid-Lowering Drugs**

Proprotein convertase subtilisin-kexin type 9 (PCSK9) is a hepatic protease that degrades hepatic LDL receptors leading to increased serum LDL-C levels. Monoclonal antibody inhibitors of PCSK9 are novel parenterally administered lipid-lowering agents that have been shown to reduce LDL by 60% to 70% when added to statin therapy. A meta-analysis of 24 randomized trials including >10000 subjects using PCSK9 inhibitors found a significant reduction in all-cause mortality (OR, 0.45; 95% CI, 0.23 to 0.86) and myocardial infarction (OR, 0.49; 95% CI, 0.26 to 0.93).57 In addition, a phase III study showed that alirocumab, one of the PCSK9 inhibitors, was associated with a 62% reduction in LDL, and this translated into a 48% decrease in the risk of major cardiovascular events. However, there was no difference in stroke risk between the treatment and the control groups (0.6% versus 0.3%; P=0.35) although the stroke risk was low. Some adverse events, including myalgias, injection site reactions, ophthalmologic events, and neuropsychiatric events (including memory impairment and confusional state), occurred more often in patients receiving alirocumab. The mechanisms of cognitive changes are uncertain, but could reflect changes in white matter integrity in the setting of extremely low LDL levels. Evolocumab is another monoclonal antibody that inhibits PCSK9 that has been shown in a randomized open trial (n=4465 patients) to be superior to standard of care (70% of which included statin therapy) in reducing cardiovascular events over a median follow-up of 11.1 months (hazard ratio 0.47; 95% CI, 0.28 to 0.78) with the similar overall serious adverse event profile (7.5% in each group). More patients on evolocumab had neurocognitive deficits (0.9 versus 0.3%), however.58 These monoclonal antibodies are currently approved by the Food and Drug Administration, but their use may be challenged by the need for injections. Randomized trials are needed to prove the safety and efficacy of alirocumab and other PCSK9 inhibitors as an add-on treatment to statins in patients with elevated LDL for primary and secondary stroke prevention, particularly in light of the potential for neurocognitive effects.

**Statins and ICH**

Although evidence suggests an inverse relationship between lipids and hemorrhagic stroke, the association between statin use and ICH remains unclear. The HPS study was the first clinical trial to show a nonsignificant increase in the risk of ICH with simvastatin versus placebo (1.3% versus 0.7%).59 In SPARCL, patients on atorvastatin were more likely to have ICH than those on placebo (2.3% versus 1.4%; P=0.01).60 A recent meta-analysis including 31 clinical trials, however, showed no increase in risk of ICH with statin use (OR, 1.08; 95% CI, 0.88 to 1.32).60 Any potential increase in risk of ICH is likely to be low, therefore.

**Guidelines on Lipid Management**

The most recent American Heart Association/American Stroke Association guidelines recommend high-intensity statin therapy for patients with ischemic stroke presumed to be related to atherosclerosis, regardless of LDL level. High-intensity statin therapy is defined as therapy sufficient to lower the LDL-C by at least 50%; no specific target values are provided any longer. The guidelines further recommend that use of statin therapy in patients with nonatherosclerotic mechanisms should be based on their overall cardiovascular risk and comorbid conditions. This is also based on the American College of Cardiology/American Heart Association guidelines that move away from reliance on LDL levels to determine the intensity of statin therapy. According to these guidelines, statin therapy is recommended to patients with (1) clinical atherosclerotic cardiovascular disease (atherosclerotic stroke or transient ischemic attack and coronary artery disease); (2) LDL-C ≥190 mg/dL; (3) age 40 to 75 years, diabetes mellitus, and LDL-C 70 to 189 mg/dL; (4) LDL-C 70 to 189 mg/dL, no diabetes mellitus, and estimated 10-year atherosclerotic cardiovascular disease risk of ≥7.5% based on the new pooled cohort equations. High-intensity statin therapy is recommended for those <75 years and at low risk of statin complications, with atherosclerotic cardiovascular disease, LDL-C ≥190 mg/dL, or diabetes mellitus and a 10-year risk of atherosclerotic cardiovascular disease of ≥7.5%. Moderate intensity statin therapy (ie, a lowering of LDL-C of 30%–50%) is recommended for other groups.

**Conclusions**

Lipids have a complex relationship with cerebrovascular disease. There is a direct relationship between cholesterol levels and ischemic stroke, and particularly atherosclerotic disease, and the associations are strongest for TC and LDL. There is an increased risk of ICH at low cholesterol levels, and there is evidence that low lipid levels also increase the risk of small vessel disease. Statins reduce the risk of recurrent stroke after ischemic stroke, but the role of adding newer lipid-lowering agents remains to be determined.

**Disclosures**

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**References**


Key Words: cerebral hemorrhage ▪ cholesterol ▪ lipids ▪ lipoprotein(a) ▪ stroke
지질과 뇌졸중 사이의 관계는 복잡하다. 대부분의 역학 연구에서 콜레스테롤 수치와 허혈뇌졸중 사이에는 직접 적인 연관성이 있다. 그러나 지질의 허혈뇌졸중에 대한 관련성은 뇌졸중의 양과 따라 다름에, 축성뇌졸중 뇌졸중 형태의 뇌졸중이 가장 관련성이 높다. 이와는 반대로 낮은 콜레스테롤 수치는 뇌졸중 위험을 증가시키고, 소혈관질환과 유사한 지질과의 역상관관계의 양상을 공유한다는 근거가 있다. 이러한 관련성은 또한 특정 지질 성분에 의해 결정되는데, 총콜레스테롤 및 저밀도지질단백질(LDL) 콜레스테롤과의 연관성이 가장 강하다. 더욱 강력한 지질강하제 사용이 가능한 점을 감안할 때, 이상지질혈증과 뇌졸중과의 관련성에 대한 이해는 일차 및 이차 뇌졸중 예방 전략을 향상시킬 수 있다.

본 논평에서 저자들은 지질 선별검사에 대한 권고 및 치료에 대한 근거기반 접근에 중점을 두어 이상지질혈증과 뇌졸중 사이의 관련성에 대한 문헌을 고찰하였다.

지질 수치와 뇌졸중의 위험
총콜레스테롤 및 저밀도지질단백질 콜레스테롤

모두 그런 것은 아니지만 대부분의 관찰연구에서 총콜레스테롤 및 LDL 콜레스테롤의 증가는 허혈뇌졸중의 위험 증가와 관련이 있다(Table 1).1-12

또한 대부분의 관찰연구에서 총콜레스테롤 및 LDL 콜레스테롤의 감소가 뇌졸중 위험의 위험 전단도에 유의한 효과는 없는 것으로 조사하였기 때문에, 일부는 총콜레스테롤과 뇌졸중의 위험 증가가 있는 것이 확인되었다.13-15

고밀도지질단백 콜레스테롤 및 고밀도지질단백질 콜레스테롤 소분획

몇몇 연구에서 HDL 콜레스테롤과 뇌졸중 사이에 역의 상관관계가 확인되었다(Table 2).16-18 10개의 전향적 연구들에 대한 계통적 고찰에서 HDL 콜레스테롤이 10 mg/dL 증가할 때마다 허혈뇌졸중의 위험에 감소하는 것이 확인되었다.21

HDL 콜레스테롤과 뇌졸중의 연관성에 대한 연구들이 역강한 결과를 보였고, 최근의 연구들은 HDL을 증가시키는 약물의 혈관내 조절이 뇌졸중 위험에 대한 유의한 효과는 없는 것으로 조사하였기 때문에, 일부는 HDL 콜레스테롤과 뇌졸중의 위험 증가와 관련이 있는 총 HDL 콜레스테롤보다는 HDL 콜레스테롤 소분획의 함수적 관계라고 해석하기도 한다. HDL 콜레스테롤은 두 가지 주요 소분획이 있다: 크고 밀도가 낮은 HDL 콜레스테롤(HDL2)과 작고 밀도가 높은 HDL 콜레스테롤(HDL3)이 그 것이다. 이러한 소분획은 생물학적 활성이나 생화학적 특성 및 혈관 내에서의 관계가 있는 반면, HDL2보다 HDL3는 더욱 LDL 산화를 억제하고 혈관내

From the Division of Stroke and Cerebrovascular Disease, Department of Neurology, The Warren Alpert Medical School of Brown University, Providence, RI (S.Y.); and Department of Neurology, College of Physicians and Surgeons and Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY (M.S.V.E.).

Correspondence to Mitchell S.V. Elkind, MD, MS, Columbia University Medical Center, 710 W 168th St, New York, NY 10032. E-mail mse13@columbia.edu

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Table 1. Lipid Profile Component and Ischemic Stroke Risk

<table>
<thead>
<tr>
<th>Lipid Profile Component</th>
<th>Study</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>Alpha-Tocopherol, Beta Carotene Cancer Prevention Study&lt;sup&gt;4&lt;/sup&gt;</td>
<td>28,000 men smokers</td>
<td>Increased risk of ischemic stroke with a total cholesterol levels ≥27 mmol/L (≥271 mg/dL; HR, 1.25; 95% CI, 0.99–1.57)</td>
</tr>
<tr>
<td></td>
<td>Asia Pacific Cohort Studies Collaboration&lt;sup&gt;4&lt;/sup&gt;</td>
<td>35,203 individuals from Asia and New Zealand</td>
<td>For every 1-mmol/L increase in total cholesterol, there was a 25% (95% CI, 13–40) increase in ischemic stroke rate</td>
</tr>
<tr>
<td></td>
<td>Women’s Health Study&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Prospective cohort study of 27,937 US women aged ≥45 y</td>
<td>Total cholesterol level was associated with ischemic stroke (adjusted HR per 1-mmol/L increase for ischemic stroke of 1.17 (95% CI, 1.06–1.30)</td>
</tr>
<tr>
<td></td>
<td>Eurostroke Project&lt;sup&gt;4&lt;/sup&gt;</td>
<td>22,183 subjects</td>
<td>No relationship between total cholesterol level and ischemic stroke</td>
</tr>
<tr>
<td></td>
<td>Women’s Pooling Project&lt;sup&gt;4&lt;/sup&gt;</td>
<td>24,343 US women &lt;55 y of age with no previous cardiovascular disease</td>
<td>Higher total cholesterol was associated with increased risk of ischemic stroke (HR, 1.69; 95% CI, 0.91–3.13, for topmost quintile compared with the lower-most one)</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>Women’s Health Study&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Prospective cohort study of 27,937 US women aged ≥45 y</td>
<td>Serum LDL cholesterol was associated with increased risk of ischemic stroke (HR, 1.74; 95% CI, 1.14–2.66; P [trend across quintiles]=0.003)</td>
</tr>
<tr>
<td></td>
<td>The Atherosclerosis Risk in Communities&lt;sup&gt;4&lt;/sup&gt;</td>
<td>14,175 middle-aged men and women without clinical cardiovascular disease</td>
<td>Nonsignificant association between LDL cholesterol and ischemic stroke (HR, 1.26; 95% CI, 0.91–1.76, for topmost quintile compared with the lower-most one)</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>Copenhagen City Heart Study&lt;sup&gt;4&lt;/sup&gt;</td>
<td>19,698 women and men at least 20 y old</td>
<td>47% reduction in the risk of nonhemorrhagic stroke for every 1-mmol/L increase in HDL</td>
</tr>
<tr>
<td></td>
<td>Northern Manhattan Stroke Study&lt;sup&gt;4&lt;/sup&gt;</td>
<td>539 patients and 905 controls</td>
<td>Inverse relationship between ischemic stroke and HDL level ≤35 mg/dL (0.91 mmol/L; OR, 0.53; 95% CI, 0.39–0.72)</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular Health Study&lt;sup&gt;4&lt;/sup&gt;</td>
<td>5,201 adults aged ≥65 living in US communities, plus a recruitment of 687 blacks 3 y later</td>
<td>Higher HDL cholesterol level was associated with a decreased risk of ischemic stroke in men, but not in women</td>
</tr>
<tr>
<td></td>
<td>The Atherosclerosis Risk in Communities&lt;sup&gt;4&lt;/sup&gt;</td>
<td>14,175 middle-aged men and women without clinical cardiovascular disease</td>
<td>No relationship between HDL cholesterol and ischemic stroke in men and a nonsignificant association in women</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>The Atherosclerosis Risk in Communities&lt;sup&gt;4&lt;/sup&gt;</td>
<td>14,175 middle-aged men and women without clinical cardiovascular disease</td>
<td>Fasting triglyceride levels were not associated with ischemic stroke</td>
</tr>
<tr>
<td></td>
<td>Physicians’ Health Study&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Men, 296 strokes and 296 controls</td>
<td>No association between triglyceride level and ischemic stroke</td>
</tr>
<tr>
<td></td>
<td>Copenhagen City Heart Study&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Prospective, population-based cohort study comprising ≈14,000 patients</td>
<td>15% (95% CI, 9–22) increased risk of ischemic stroke for each 89-mg/dL increase in nonfasting triglycerides</td>
</tr>
<tr>
<td></td>
<td>Women’s Health Study&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Prospective cohort study of 27,937 US women aged ≥45 y</td>
<td>The highest tertile of nonfasting but not fasting triglyceride level was associated with increased ischemic stroke risk when compared with lowest tertile</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; HDL, high-density lipoprotein; HR, hazard ratio; and LDL, low-density lipoprotein.
서 10 mg/dL 증가한 때마다 뇌졸중의 상태위험도가 증가하였는데(보정 상태위험도, 1.05; 95% CI, 1.03–1.07), 이 분석에서는 공복 및 비공복 상태를 명시하지 않았다. 몇몇 연구들은 증상지 방 수치와 출혈뇌졸중의 위험이 억의 상관관계가 있다고 제시하였다(Table 2). 16,17

지질단백질(a) (Lp(a))

지질단백질(a) (이하 Lp(a))은 심혈관질환에 대한 새로운 위험 인자로 확인되었다. 혈중 Lp(a)의 수치는 유전적인 요인이 의해 영향을 받으며 인종간에 두려한 차이를 보이기도 하며 가장 높다.26 Lp(a)와 뇌졸중의 위험과의 관계에 대한 연구들의 결과는 엇갈린 결과를 보여주었다. 15,000명의 건강한 백인 중년을 주요 대상으로 시행한 코호트 내 한자 대조군 연구 결과 Lp(a)의 수치와 뇌졸중의 위험과의 관계가 없었다.27 유럽의 코호트 연구에서도 혈청 내 Lp(a)의 수치는 허혈뇌졸중과는 관련이 없었다.28이상지질혈증과 큰동맥죽상경화증에 의한 뇌졸중의 관련성이 더 크기 때문에(교차비 3.2), 이상지질혈증과 큰동맥죽상경화증으로 인한 뇌졸중의 관

관성은 다른 연구들에게서도 제시되었다.29,30

이와는 반대로 모든 연구에서 이상지질혈증과 열공뇌졸중과의 관련성이 제시되지 않았다. 화자대조군 연구들에서 콜레스테롤31과 LDL 콜레스테롤32가 열공뇌졸중과 관련이 있다고 보고되었다. 그러나 다른 연구에서는 이상지질혈증과 열공뇌졸중과의 관련성을 보이지 않았다.33,34 그러므로 이상지질혈증과 열공뇌졸중의 관련성은 복잡하고 다양한 환자군에서의 유전적 및 인구학적 요인 및 뇌졸중 이행을 어떻게 정의하는지에 따른 차이에 의해 영향을 받을 수 있다. 이상지질혈증은 관상동맥질환의 위험인자이며, 대부분의 연구에서 이상지질혈증과 백질고신호강도병변과의 관

관성은 제시되지 않았다.31-33

지질, 백질변성 및 대뇌미세출혈

백질고신호강도, 또는 백질변성은 연령, 고혈압 및 흡연과 같은 뇌졸중의 위험인자와 관련이 있다.35 백질고신호강도, 대뇌미
세출혈 및 심부 뇌세출혈은 소혈관질환의 다양한 양상으로 간주되고 있기 때문에, 지질과 백질고신호강도 및 대뇌미세출혈 사이의 관련성은 지질과 소혈관질환과의 관련성을 설명하는데 도움이 될 수 있다. 실제로 이상지질혈증과 백질고신호강도간의36,37 및 대뇌 미세출혈38의 관련성은 억의 상관관계가 있다는 연구들

이 있어 지질 수치를 낮추는 것이 소혈관의 구조 또는 기능을 손상시킬 수 있다는 근거를 제시한다. 이상은 종합한 때 위의 자료들은 소혈관질환(백질고신호강도 및 대뇌미세출혈)과 고지혈증 사이에는 억의 상관관계에 대한 일부 근거를 제공한다. 이것은 콜레스테롤이 작은 혈관의

<table>
<thead>
<tr>
<th>Table 2. Lipid Profile Component and Hemorrhagic Stroke Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid Profile Component</td>
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<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>Total cholesterol</td>
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<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>LDL Cholesterol</td>
</tr>
<tr>
<td>Triglycerides</td>
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<td></td>
</tr>
</tbody>
</table>

ARIC indicates Atherosclerosis Risk in Communities; CI, confidence interval; HDL, high-density lipoprotein; HR, hazard ratio; and LDL, low-density lipoprotein.
뇌졸중 이후의 지질 수치에 대한 선별검사

혈청 내피세포는 혈관내피세포의 구조 및 온전함에 대한 역할에 관련이 있을 수 있고 따라서 낮은 지질 수치가 내피세포의 온전성을 방해하고 내피세포의 재생과정에 손상을 입으며 작은 혈관의 유출 및 폐색을 유발할 수 있다. 이와 관련한 정확한 기전은 아직 명확하지 않아 더 많은 연구가 필요하다.

뇌졸중은 혈청 총콜레스테롤, LDL 및 HDL 콜레스테롤의 증가와 중성지방의 증가에도 불구하고 간이 정상인 경우에 대한 검사가 수행되어야 한다. 이와는 반대로 증가가 많지 않은 경우 감안할 때 Lp(a) 및 HDL 소분획에 대한 지질성분 검사를 정기적으로 시행하는 것은 추천되지 않는다.

지질성분검사에서 보고되는 LDL 콜레스테롤 수치는 일반적으로 Friedewald 공식을 사용하여 계산된다.43

\[
\text{LDL-C} = \text{TC} - (\text{very low-density lipoprotein-cholesterol} + \text{HDL-C})
\]

비공복상태의 환자에서는 식후 혈중의 킬로미크론이 총콜레스테롤 수치에 기여하여 측정이 정확하지 않기 때문에 이 공식은 공복상태에서 더욱 정확하다. 또한 이러한 방법은 중성지방이 400 mg/dL 이상인 경우 부정확하고, LDL 콜레스테롤 농도가 70 mg/dL 이하이면 더 높은 오차 범위를 가진다.44 LDL 콜레스테롤의 직접적인 측정법이 콜레스테롤 수치 측정을 위해 개발되었다. 직접 측정은 Friedewald 공식을 사용하는 경우에 비해 훨씬 더 정확이지만, LDL 콜레스테롤 농도를 계산하기 위해 필요할 수 있다. 그러나 대부분의 임상시험 및 지질치료지침은 계산하여 추정된 LDL 콜레스테롤 수치에 기반하고 있다.

뇌졸중 이후에 지질검사를 시행하는 시점은 심근경색 이후에 지질검사를 연중 행한 것인가에 비해 몇 훨씬 높다. 낮은 지질 수치의 변화는 심근경색 이후의 경우처럼 급격히 감소하지는 않는다는 근거이다.45 더구나 300,000명 이상의 환자들이 포함된 68개 연구들을 분석한 메타연구에서 심장비교적과 병증, 비공복성의 환자들에서 측정되었을 경우에도 지질성분과 혈관의 관계성이 차이나다고 보고되었다.46 앞서 언급한 바와 같이 이에 대한 지질성분의 관계성은 비공복상태에서 측정된 경우 더욱 현저하다. 그러므로 지질성분은 우선적으로 공복상태에서 측정을 훨씬 더 정확하게 지질성분에서 측정될 수 있으며, 적어도 총콜레스테롤, LDL 및 HDL 콜레스테롤을 포함해야 한다.

지질강하치료와 뇌졸중

뇌졸중 일차예방에서 스타틴 치료

심혈관질환에서의 유용성을 더하여 스타틴은 뇌졸중 위험 감소에도 명확한 효용성을 갖고 있다. 뇌졸중의 일차예방 임상시험에서 여러 스타틴들은 뇌졸중의 위험을 11-40% 정도 감소시켰다. The Heart Protection Study (HPS)에서는 20,000명 이상의 성인 40세에서 80세 사이의 혈관질환 고위험 환자들을 simvastatin 40 mg 하루 한 번 투여군과 위약군으로 무작위 할당하였다. 이 연구에서는 스타틴의 투여가 출혈뇌졸중의 위험 증가 없이 뇌졸중 위험을 25% 감소할 수 있었다.50 더 적극적인 치료는 뇌졸중 위험을 더 낮추었다. Treating to New Targets (TNT) 연구에서 하루 한 번 atorvastatin 10 mg 투여와 비교하여 80 mg 투여는 뇌졸중 위험을 25% 낮추었고 이는 LDL 콜레스테롤 감소와 연관이 있었 다. 뇌졸중 이후의 지질수치에 대한 메타분석에서 LDL 콜레스테롤이 1 mmol/L 감소할 경우 허혈뇌졸중의 상대위험도가 20% 감소하였다.46,47

뇌졸중의 이차예방에서의 스타틴 치료

HPS 연구의 사후분석에서 관상동맥질환의 병력이 있는 3,280명의 환자들에서 simvastatin 투여는 위약 대비 주요 심혈관사건 혹은 사망을 5% 감소시켰다.48 그러나 Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) 연구는 뇌졸중의 이차예방에 있어 스타틴의 역할에 대한 가장 직접적인 근거를 제공하였다. SPARCL 연구에서는 4,731명의 뇌졸중 혹은 일과성허혈발작으로 진단된 환자들이 발생 1-6개월 내에 atorvastatin 80 mg 투여군과 위약군으로 무작위 배정하였다. 평균 5년 간의 추적관찰 동안 atorvastatin 투여는 전체 뇌졸중 예방 위험을 약 15% 정도 감소시켰다.49,50 스타틴의 뇌졸중 위험 감소에 대한 효과는 최초 뇌졸중의 소그룹을 아형과 무관하게 얻을 것으로 보이고, 뇌졸중의 소그룹 아형과 상관없이 허혈뇌졸중을 가진 모든 환자들은 스타틴 치료를 받아야 한다는 것을 시시하였다. 그러나 현재의 전문학회의 지침은 조건부로만 추천하여 스타틴 치료는 고용량의 스타틴치료가 뇌졸중의 이차예방에 효과적임을 증명한 최초의 연구로 5년 이상 기간 동안 50명을 치료해야 그 효과를 기대할 수 있는 수준이라고. 그러나 SPARCL 연구는 몇 가지 제한점을 가지지만, 스타틴 치료는 고용량의 스타틴치료가 뇌졸중의 이차예방에 있어 효과적임을 증명한 최초의 연구라고 그 효과가 시간이 지남에 따라 낮아지지 않아 5년 이상 기간 동안 50명을 치료해야 그 효과를 기대할 수 있다는 주장을 반영한 것이다.51 SPARCL 연구는 고용량의 스타틴치료가 뇌졸중의 이차예방에 있어 효과적임을 증명한 최초의 연구라고 그 효과가 시간이 지남에 따라 낮아지지 않아 5년 이상 기간 동안 50명을 치료해야 그 효과를 기대할 수 있는 수준이라고. 그러나 SPARCL 연구는 몇 가지 제한점을 가지하지만, 스타틴 치료는 고용량의 스타틴치료가 뇌졸중의 이차예방에 있어 효과적임을 증명한 최초의 연구라고 그 효과가 시간이 지남에 따라 낮아지지 않아 5년 이상 기간 동안 50명을 치료해야 그 효과를 기대할 수 있는 수준이라고.
고 있다. 예를 들어 환자들은 뇌졸중 발생 후 1~6개월 이내에 무작위 배정 되었는데, 이 기간은, 특히 스타틴의 뇌졸중 예방 효과 제일 큰 고혈압성경화증을 가진 환자에서, 뇌졸중의 재발위험 이 낮아지는 기간이었다. 현재 진행 중인 연구는 뇌졸중 직후 스타틴 치료의 효과를 강조하고 있는데, 지질 수치를 낮추어 뇌졸중의 재발위험이 낮아지는 기간이었다. 현재 진행 중인 연구는 뇌졸중 직후 스타틴 치료의 효과를 강조하고 있는데, 지질 수치를 낮추어 뇌졸중 재발 위험을 예방하는 것과 함께 뇌졸중 자체에 의한 뇌손상을 개선할 수 있는지에 대해서도 연구되고 있다. 예를 들면 Neuroprotection with Statin Therapy for Acute Recovery (NeuSTART) 연구는 2상 임상시험으로 급성뇌졸중 환자들에게 3일간 640 mg의 lovastatin을 무작위로 지정한 군과 위약군으로 무작위 할당하여 lovastatin의 안정성과 스타틴의 발현적 효과로 여겨지는 뇌졸중 크기의 감소 및 뇌졸중 회복의 증진에 효과를 비교하기 위해 연구가 진행되고 있다.50 또 다른 제한점으로 SPARCL 연구는 목표 LDL 수치를 설정하지 않았다.

지질 조절 이외의 스타틴 치료

연구자들은 스타틴의 유용한 다면 발현적 효과가 간에서 콜레스테롤 대사에 대한 기전과는 다른 기전에 의할 수 있다고 제시한다. 이러한 다른 잠재적인 기전으로는 염증반응 단계 억제, 항산화효과, 산화질소 합성효소의 상향조절 및 이에 기인한 뇌혈류 증가, 콩적혈관의 안정 및 혈소판고와 혈소판 기능에 대한 조절효과 등이 제시되고 있다. 이러한 기전들은 뇌졸중의 예방뿐만 아니라 급성뇌졸중에서 기능적 예후 향상에도 기여할 수 있다.

뇌졸중의 예방에서 기타 지질저하제

뇌졸중의 일차 및 이차 예방에 대한 스타틴 이외의 지질저하제의 효용성은 아직 확립되지 않았다. Niacin의 경우, HDL 콜레스테롤 수치를 증가시킬 수 있으며, 혈관질환의 감소에 대한 효과는 아직 불명확하다. 11개 연구의 메타분석(9,559명을 대상)에서는 niacin의 사용과 뇌졸중의 위험은 관련성을 보이지 않았다(교차비, 0.88: 95% CI, 0.50–1.54).54 피브릭산 유도체는 중성지방을 낮추고 HDL 콜레스테롤을 증가시킬 수 있으나, 뇌졸중 발생 감소에 대한 효과는 명확하지 않다. Veterans Affairs–HDL Intervention Trial (VA–HIT) 연구에서는 관상동맥질환을 가진 남성에서 HDL 콜레스테롤이 낮은 경우 benzbobibrate 투여가 뇌졸중의 위험을 31% 감소시켰다(P=0.038).55 그러나 18개의 연구를 포함하여 45,000명 이상의 환자를 대상으로 한 메타분석에서는 fibrates가 뇌졸중의 위험을 감소시킨다. 근거를 제시하지 못하였다(상대위험도 감소, -0.3%: 95% CI, -16 – 9%).53 Ezetimibe은 장에서의 콜레스테롤 흡수를 억제하여 콩적コレ스 telesc을 감소시킨다. 최근에 보고된 Improved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) 연구에서는 하루 한 번 simvastatin 40 mg의 투여에 대하여 ezetimibe 10 mg을 투여한 것이 뇌졸중의 위험을 유의하게 감소시켰다(위험도, 0.86: 95% CI, 0.73–1.00).54

지질강화제에 대한 78개의 연구를 포함한 메타분석에서 fibrate, 다른 지질 및 식이요법을 포함한 비스타틴 지질강화요법은 뇌졸중 위험감소에 유한한 효과를 보이지 않았다(교차비, 0.92: 95% CI, 0.69–1.23).55

사으로운 지질강화제

Proprotein convertase subtilisin–kexin type 9 (PCSK9)은 간 LDL 수용체를 분해하는 간 단백질로 혈청 내 LDL 콜레스테롤 농도 증가로 이어진다. PCSK9의 단클론항체 약제는 비정구용으로 투여되는 새로운 지질저하제로 스타틴 치료와 병합하였을 경우 LDL 콜레스테롤의 농도를 60–70% 감소시킨다.56 24개의 연구 10,000명 이상의 환자를 대상으로 한 메타분석에서 PCSK9 약제는 모든원인사망을 감소시키고(교차비, 0.45: 95% CI, 0.23–0.86), 심근경색 위험을 감소시켰다(교차비, 0.49, 95% CI, 0.26–0.93)57. 또한 3상 임상시험에서 PCSK9 억제제의 하나인 alirocumab은 LDL 콜레스테롤을 62% 감소시켜 주요 심혈관질환 사건의 위험을 48% 감소시키는 것으로 보고되었다. 그러나, 비록 뇌졸중 위험이 낮기는 하였지만 치료군과 대조군 사이의 뇌졸중 위험은 차이가 없었다(0.6% vs. 0.3%, P=0.35), 극복력, 주사부위 통증, 약과 관련 사건 및 신경인지지가(기억력 저하 및 혼돈 상태 포함)는 alirucumb을 투여 받은 환자군에서 더 많이 발생하였다.58 인지기능 변화의 기전은 명확하지 않지만 상당히 낮은 LDL 콜레스테롤 상태에서 백질의 온전성의 변화를 반영했을 수 있다. Evolocumab은 PCK9를 저해하는 단클론항체로 4,465명을 대상으로 한 무작위 임상시험에서 표준치료(70%는 스타틴 치료를 포함)과 비교하여 11개월의 추적관찰 기간 동안 심혈관질환 사건 발생 감소에 대해 유의하였고(위험도 0.47: 95% CI, 0.28–0.78), 전반적인 심혈관사망에 비슷하였다(각 군당 7.5%). 그러나 evolocumab을 투여 받은 환자에서 심장뇌경질의 발생이 증가하였으나(상대위험도 1.79; 95% CI, 1.29–2.49), 이들의 심혈관질환 사망은 매우 적었다(각 군당 7.5%).59

스타턴과 뇌내출혈

지질과 출혈뇌졸중 사이의 역의 상관관계를 제안하는 근거들은 있지만, 스타틴의 사용과 뇌내출혈의 연관성은 불명확하다. HPS 연구는 위약 대비 simvastatin의 투여가 뇌내출혈의 위험 증가와 통계적으로 유의하지 않지만 증가된 위험(1.3% vs. 0.7%)
을 보여준 최초의 연구이다. SPARCL 연구에서 atorvastatin을 투여받은 환자들은 위약을 투여받은 환자들에 비해 뇌내출혈의 발생이 많았다 (2.3% vs. 1.4%; P=0.01). 그러나 31개 연구를 포함한 최근의 메타분석에서는 스타틴의 사용이 뇌내출혈의 위험을 증가시키지 않았다 (교차비, 1.08; 95% CI, 0.88-1.32). 그러므로 잠재적인 뇌내출혈 위험 증가는 낮을 것으로 간주된다.

지질치료에 대한 지침

미국심장협회/미국뇌졸중협회의 가장 최신의 지침에서는 LDL 수치에 상관없이 죽상경화증과 관련되어 있을 것으로 보이는 혈뇨증중 환자들에게 고강도 스타틴 치료를 추천하고 있다. 고강도 스타틴 치료는 LDL 콜레스테롤을 적어도 50% 이상 감소시키기에 충분한 치료로 정의하고 있지만 특정 목표를 제시하고 있지 않다. 이 지침지침은 또한 비죽상경화성 기전을 가진 환자들에 대한 스타틴 치료를 전반적인 심혈관위험도 및 동반질환을 고려하여 결정이 되어야 한다고 권고하고 있다. 이것은 또한 미국심장협회/미국뇌졸중협회의 권고에 기초한 것으로 스타틴 치료의 강도 결정에 있어 LDL 콜레스테롤 수치에 의존하던 것에서 벗어난 것이다.

결론

지질은 뇌혈관질환과 복잡한 관련성을 갖고 있다. 콜레스테롤 수치와 허혈뇌졸중, 특히 죽상경화성뇌졸중의 위험을 늘리고 있다는 점에서 중요하다. 그러나 스타틴 치료의 효과는 아직도 논란의 여지가 있다. 스타틴 치료는 뇌졸중 재발 위험을 낮추는 데 성공했지만, 새로운 지질간호학적 치료의 효과를 아직 확실하지 않다.

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