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Stroke Linked to Cholesterol in Otherwise Healthy Women

By Crystal Phend, Staff Writer, MedPage Today
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 February 20, 2007



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BOSTON, Feb. 20 -- Even healthy women with no history of heart disease or stroke need to keep their cholesterol down to help head off stroke risk, researchers here said.

Action Points

- Explain to interested women that their stroke risk is higher if they have elevated cholesterol levels even if other risk factors such as history of heart disease are not present.
- The primary prevention guidelines of the American Heart Association and American Stroke Association recommend avoiding unfavorable cholesterol levels to help to prevent ischemic stroke.

In the latest analysis of the Women's Health Study, women with the highest total cholesterol levels were at more than twice the stroke risk of those with the lowest lipid levels, reported Tobias Kurt M.D., Sc.D., of Brigham and Women's Hospital, and colleagues, in the Feb. 20 issue of *Neurology*.

The results suggest that physicians should consider lipid-lowering strategies for women with elevated levels even if the patients have no history of heart disease and appear healthy, they said.

The prospective cohort study included 27,937 apparently healthy female healthcare professionals, ages 45 and older (mean 54.7) who were randomized to low-dose aspirin and vitamin E to assess primary prevention of heart disease and cancer.

The analysis by Dr. Kurth and colleagues looked specifically at ischemic stroke incidence over the 11-year follow-up period together with baseline lipid levels from blood samples submitted by the women.

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The researchers confirmed 282 ischemic strokes during this period for an occurrence rate of 9.2 per 10,000 women per year (95% confidence interval 8.2 to 10.3).

The results were controlled for randomized treatment assignments, alcohol consumption, exercise, smoking, body mass index, family history of heart attack, current postmenopausal hormone use, history of diabetes, migraine and migraine aura status, and cholesterol lowering medication use.

Compared with women in the lowest lipid level quintile, the ischemic stroke risk of those in the highest quintile was significantly elevated almost uniformly. The hazard ratio results were:

- 2.27 for total cholesterol (95% CI 1.43 to 3.60, *P* for trend=0.001),
- 1.74 for low density lipoprotein cholesterol (LDL, 95% CI 1.14 to 2.66, *P* for trend=0.003),
- 0.78 for high density lipoprotein cholesterol (HD, 95% CI 0.52 to 1.17, *P* for trend=0.27),
- 1.65 for total cholesterol to HDL ratio (95% CI 1.06 to 2.58, *P* for trend=0.02), and
- 2.45 for non-HDL (95% CI 1.54 to 3.91, *P* for trend=0.001).

Further control for systolic blood pressure and antihypertensive medication slightly attenuated these risks, but the trends for mean total cholesterol, LDL, and non-HDL remained significant.

For lipid levels as categorized by the Expert Panel on Detection, Evaluation, and Treatment of High Cholesterol in Adults (ATP III), the adjusted hazard ratios for ischemic stroke were:

- 1.70 for total cholesterol 240 mg/dL or higher versus less than 200 mg/dL (95% CI 1.24 to 2.33, *P* for trend=0.001),
- 1.59 for LDL-C 160 mg/dL or higher versus under 100 mg/dL (95% CI 1.06 to 2.39, *P* for trend=0.003), and
- 0.78 for HDL-C 60 mg/dL or above versus 40 mg/dL and under (95% CI 0.54 to 1.13, *P* for trend=0.23).

Again, controlling for systolic blood pressure and

antihypertensive medication use attenuated these risk estimates, but the trends for total cholesterol and LDL remained significant.

Interestingly, current postmenopausal hormone use did attenuate this association (P for interaction=0.02), "suggesting that women who used postmenopausal hormones did not have increased risk of ischemic stroke with increasing total cholesterol categories."

When the investigators evaluated lipid levels as continuous measure, they found:

- A 1.17-fold increase in stroke risk with each 1 millimol/l increase in total cholesterol (95% CI 1.06 to 1.30, $P=0.003$),
- A 1.15-fold increase in stroke risk with each 1 millimol/l increase in LDL (95% CI 1.01 to 1.31, $P=0.029$),
- A nonsignificant 0.91-fold decrease in stroke risk with each 1 millimol/l increase in HDL (95% CI 0.64 to 1.28, $P=0.58$), and
- A 1.19-fold increase in stroke risk with each 1 millimol/l increase in non-HDL (95% CI 1.07 to 1.32, $P=0.001$).

The strongest predictor of ischemic stroke was non-HDL ($P=0.001$) followed by total cholesterol ($P=0.004$).

However, the researchers acknowledged that the study was limited in having only one measurement of lipid levels per woman and by the lack of data on subsequent use of cholesterol lowering medication during follow-up.

Also, because most of the women (94.5%) were white, the researchers noted that the findings may not generalize to more diverse populations. But, there is no reason to believe that the biologic mechanisms of high cholesterol levels would be different in other populations, they said.

Previous studies have established a link between lipids and coronary heart disease, but the evidence for ischemic stroke was less clear and studies in this area typically included only men or individuals with pre-existing coronary heart disease.

The researchers concluded that their data along with that of

previous studies "strongly support the notion that lipids are a biologic risk factor for ischemic stroke and that avoiding unfavorable cholesterol levels may help to prevent ischemic stroke as recommended [in] the primary prevention guidelines of the American Heart Association/American Stroke Association."

The Women's Health Study is supported by grants from the National Heart, Lung, and Blood Institute and the National Cancer Institute. The analysis was supported by grants from the Donald W. Reynolds Foundation and the Leducq Foundation. The researchers reported no conflicts of interest.

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