# More Evidence Links High Cholesterol to Lower Parkinson's Risk

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VANCOUVER — Higher levels of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) are associated with a decreased risk for Parkinson's disease (PD) in men, a large observational study shows.

The results represent the latest research linking higher cholesterol with lower risk for PD.

The new findings suggest that a "one-size-fits-all" approach in clinical practice "overlooks the possible benefits" of higher serum cholesterol levels in some patients, study author Chava Peretz, PhD, professor, School of Public Health, Faculty of Medicine, Tel Aviv University, Israel, told *Medscape Medical News*.

"Tailoring individualized therapeutic strategies based on stratifying risk and personal background is important," he said.

Dr Peretz's research team presented their study at the International Congress of Parkinson's Disease and Movement Disorders (MDS) 2017.

Higher levels of serum cholesterol are well-established risk factors for coronary artery disease and stroke, but whether cholesterol levels have a similar effect in PD "remains elusive," said Dr Peretz.

"Previous studies on cholesterol and PD risk ignored the changes in cholesterol levels over time, considered only a fixed one-time cholesterol measure, and used small samples. Our study is a big-data study that included a large-scale cohort with a long follow-up time."

For the study, researchers accessed data covering 1999 to 2012 from the Maccabi Healthcare Services, a large Israeli healthcare organization serving 25% of the country's population.

The study included 261,638 persons aged 40 to 79 years not taking statins. They were followed from baseline to death, end of study, or PD diagnosis.

From annual blood tests, researchers collected information on levels of TC, LDL-C, and high-density lipoprotein cholesterol (HDL-C).

They categorized TC levels into upper (210 mg/dL or more), middle (180 to 209 mg/dL), and low tertiles and LDL-C levels into upper (140 mg/dL or more), middle (110 to 139 mg/dL), and low tertiles.

Investigators used Cox proportional hazard models with time-dependent covariates (cholesterol levels) to estimate the hazard ratio (HR) for PD. They stratified results by age and sex.

During a mean of 7.9 years, PD was diagnosed in 0.3% of participants aged 40 to 64 years and in 3.3% of those aged 65 years and older.

Among men, compared with low levels, middle and upper levels of TC and LDL-C were significantly associated with lower risk for PD. For TC, the age-pooled HR was 0.91 (95% confidence interval [CI], 0.83 - 1.04), and for LDL-C, the pooled HR was 0.86 (95% CI, 0.76 - 0.97).

## Possible Mechanisms

Several factors might explain the link between serum cholesterol and PD risk in men, said Dr Peretz.

It's possible, for example, that cholesterol plays a role via mechanisms operating in peripheral organs where PD begins, such as the gut. Another mechanism could be through the apolipoprotein E ε2 allele (*APOE* ε), which is associated with both sporadic PD and lower levels of serum LDL-C.

"It's also conceivable that lower cholesterol levels are markers of lifestyle changes that pave neurodegenerative processes years before diagnosis," said Dr Peretz.

There were insignificant associations between both TC and LDL-C levels and PD risk among women in the study. It's not clear why the association would exist in men but not women.

"The mechanisms underlying the link between higher cholesterol and lower PD risk in men are unclear and warrant further investigation," said Dr Peretz. However, the modulatory effects of sex-related hormones and of *APOE* phenotype should be considered, he added.

In both sexes, HDL-C had null results for PD risk.

## Confirms Prior Research

Commenting on these results, Xuemei Huang, MD, PhD, professor and vice chair of neurology, and professor of neurosurgery, pharmacology, radiology, and kinesiology, Penn State University, Hershey, Pennsylvania, said the new research confirms his own extensive work on this connection that dates back over a decade.

"This abstract is the latest study to confirm our original findings of the apparent paradox of higher total/LDL-cholesterol being associated with lower risk and prevalence of PD," he told *Medscape Medical News*.

"From what I can see, the novelty in this study is that it has a large population of subjects in a new cohort who did not use statins."

Dr Huang and his research colleagues first presented data showing that higher cholesterol was associated with lower prevalence of PD at the American Academy of Neurology (AAN) Annual Meeting in 2005.

The manuscript was rejected by several high-profile journals over the next few years, said Dr Huang. "I believe this was largely because our hypothesis ran counter to statins being 'wonder drugs'."

However, the paper was finally published in 2007.

In the meantime, a prospective study from the Netherlands, published in 2006, supported Dr Huang and his research team's original conclusion, and the literature continues to grow.

"We have published two prospective studies showing that it was the premorbid cholesterol that was associated with the risk," said Dr Huang.

His team's latest paper, published earlier this year, showed that statins themselves are a likely risk factor.

This new research from Israel "left open the question of what was happening in the statin users in their population and, in any event, what possible mechanism was involved," commented Dr Huang.

*The study was part of a PhD thesis by first author Violet Rozani, PhD, who had a 2-year scholarship from TEVA Company (NNE). The study received no other funding. Dr Peretz and Dr Huang have disclosed no relevant financial relationships.*

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