

Smoking, High Blood Pressure, and Diabetes May Lead to Dementia

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September 1, 2009 — Middle-aged people who smoke or have high blood pressure or diabetes are more likely to develop dementia later in life, a new study shows. In an article published online August 19 in the *Journal of Neurology, Neurosurgery and Psychiatry*, researchers suggest that controlling cardiovascular risk factors in midlife may prevent dementia later on.

"Our study population included both whites and African Americans," lead author Alvaro Alonso, MD, from the University of Minnesota in Minneapolis, told *Medscape Neurology*. "We were able, for the first time, to show that cardiovascular risk factors in midlife are associated with dementia later in life in both racial and ethnic groups."

Overall, blacks had a 2.5 times higher rate of hospitalization for dementia than whites. Black women in particular had the highest rates of all.

High Risk

Current smokers were 70% more likely than those who had never smoked to develop dementia. People with high blood pressure were 60% more likely than those without high blood pressure to develop dementia, and people with diabetes were more than twice as likely as those without diabetes to experience cognitive impairment.

The researchers also demonstrated that cardiovascular risk factors measured earlier in life are better predictors of dementia than risk factors measured in older age. "These results, again, support the need for paying special attention to cardiovascular risk factors in midlife," Dr. Alonso said.

Investigators studied more than 11,000 people who were part of the Atherosclerosis Risk in Communities (ARIC) study. Participants were aged 46 to 70 years and underwent a physical examination and cognitive testing. Patients were followed up for more than a decade to see how many would later develop dementia.

Researchers identified 203 patients hospitalized with dementia. Smoking, high blood pressure, and diabetes were all strongly associated with this diagnosis.

Cardiovascular Risk Factors Associated with Dementia

Risk Factor	Hazard Ratio	95% Confidence Interval
Smoking	1.7	1.2 to 2.5
Hypertension	1.6	1.2 to 2.2
Diabetes	2.2	1.6 to 3.0

In analyses including updated information on risk factors during follow-up, the hazard ratio of dementia in hypertensive vs nonhypertensive participants was 1.8 at age 55 years compared with 1.0 at age 70 years or older. Researchers observed similar results for diabetes, with a hazard ratio of 3.4 at age 55 years and 2.0 in

those older than 70 years. For smoking, the hazard ratio was 4.8 at age 55 years and 0.5 in patients aged 70 years or older.

"We were only able to identify individuals with dementia who were attended in a hospital," Dr. Alonso pointed out. "Therefore, it is very likely that we missed some people with dementia. Still, we did a number of additional analyzes to determine whether this could bias our results. Overall, we are confident that this limitation is not having a major impact in our overall conclusions."

The authors point to another criticism that could explain the study results. "An unmeasured factor in our population could be associated with the presence of cardiovascular risk factors and also increase the risk of dementia," Dr. Alonso added. For example, a genetic marker that increases both the risk for hypertension and dementia could be at play. "This is a possibility," he said, "but in our analysis, we adjusted for the most important variables associated with cardiovascular risk factors and dementia, including some genetic factors such as apolipoprotein E."

Bad for the Heart, Bad for the Brain

In the August issue of *Dementia and Geriatric Cognitive Disorders*, researchers came to a similar conclusion and reported that elevated cholesterol in midlife may increase dementia risk (*Dement Geriatr Cogn Disord*. 2009;28:75–80).

As previously reported by *Medscape Neurology*, lead author Alina Solomon, MD, from the University of Kuopio, Finland, used data from the Kaiser Permanente Northern California Medical Group to investigate the relationship between cholesterol and dementia and found that even cholesterol levels of 200 to 239 mg/dL could increase risk.

"Both physicians and patients need to know that elevated cholesterol increases the risk not only for heart disease, but also for dementia," Dr. Solomon said.

During an interview when the Solomon study was first released, Robert Stewart, MD, from King's College London in the United Kingdom, said that the data are convincing and consistent with those from other studies that have screened community populations for this disorder.

"In general," Dr. Stewart said, "there is now a large body of evidence which indicates that what is bad for the heart is bad for the brain — that is, that the well-known risk factors for coronary heart disease and stroke are also risk factors for dementia."

The ARIC study was funded by the National Heart, Lung and Blood Institute. The researchers have disclosed no relevant financial relationships.

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Clinical Context

Dementia has a profound impact on individual patients, their loved ones, and society as a whole. In the United States, the burden of dementia is expected to grow worse, and the authors of the current study review the epidemiology of dementia in the United States. Currently, approximately 1 in 6 individuals older than 70 years has dementia, and the prevalence of dementia is expected to increase 3-fold between 2000 and 2050. Alzheimer's disease is the most common cause of dementia, accounting for 70% of cases, whereas vascular

disease causes approximately 20% of dementia. Other illnesses promote the remaining 10% of dementia cases.

Previous research suggests that traditional cardiovascular risk factors may be independent predictors of dementia, but this evidence is counterbalanced by research findings that controlling chronic illness, such as maintenance of normal blood pressure levels among older adults with hypertension, fails to reduce the risk for dementia. The current study examines a large cohort of adults followed up for more than a decade to better understand the relationship between cardiovascular risk factors and the incidence of dementia.

Study Highlights

- The ARIC trial enrolled adults between 45 and 64 years old. The original study recruitment occurred between 1987 and 1989. Participants were examined approximately every 3 years after enrollment until 1996 to 1998.
- The current analysis focused on patients who underwent a history and physical examination between 1990 and 1992. Participants also had a laboratory evaluation, including genotype testing for apolipoprotein E.
- Participants with a history of coronary heart disease, stroke, transient ischemic attack, or evidence of dementia at baseline were excluded from study analysis.
- The main study outcome was the effect of traditional cardiovascular risk factors on the incidence of hospitalization for dementia. Researchers used hospital discharge billing data to find cases of dementia.
- The main study outcome was adjusted to account for demographic factors as well as the presence of other cardiovascular risk factors and the apolipoprotein E genotype.
- 11,151 individuals met criteria for study analysis. The mean age of participants was 56 years old at study entry, and 23% of participants were African American.
- African Americans had higher rates of hypertension, diabetes, and obesity vs Caucasians.
- Researchers recorded 203 cases of hospitalization for dementia during 142,625 person-years of follow-up. The mean age at first hospitalization was 71.7 years.
- African Americans had higher rates of dementia vs Caucasians.
- The presence of the apolipoprotein $\epsilon 4$ allele was associated with an 80% increase in the risk for dementia, and there was a dose-dependent positive relationship between the number of apolipoprotein E alleles and the risk for dementia.
- Smoking (hazard ratio, 1.7), hypertension (hazard ratio, 1.6), and diabetes (hazard ratio, 2.2) were all associated with an increased risk for dementia. These risks were similar among African Americans and Caucasians. However, obesity/overweight and hypercholesterolemia were not associated with increased dementia risk.
- The risk for dementia associated with smoking, diabetes, and hypertension was most significant among adults who reported these variables between the ages of 55 and 69 years. The risk for dementia associated with these variables after age 70 years was not significant.

Clinical Implications

- Currently, approximately 1 in 6 US adults older than 70 years has dementia, and the prevalence of dementia is expected to increase 3-fold in the United States between 2000 and 2050. Alzheimer's disease is the most common cause of dementia, accounting for 70% of cases, whereas vascular disease causes approximately 20% of dementia.

- In the current study, smoking, diabetes, and hypertension were associated with a higher risk for hospitalization for dementia, but obesity and hypercholesterolemia were not.