

# Comorbid Depression Can Double Risk of Dementia

*Adverse synergy is marked by sedentary lifestyle, nonadherence, and lower levels of self-care.*

BY DAMIAN McNAMARA

EXPERT ANALYSIS FROM THE ANNUAL MEETING OF THE AMERICAN PSYCHIATRIC ASSOCIATION

HONOLULU – Diabetes can be a challenge to control, depression can be difficult to treat and keep in remission, and growing evidence suggests the combination can be especially problematic for patients. And as if this adverse synergy were not bad enough, having these two conditions more than doubles the likelihood that a patient will develop dementia, Dr. Wayne J. Katon said.

Screening all patients with type 2 diabetes for depression, therefore, could have a big impact, he said at the meeting. The American Diabetes Association has endorsed such screening since 2005.

Given the bidirectional relationship between these conditions, physicians treating patients with depression also should assess, counsel, and monitor them for the development of diabetes. “Some of our psychiatric education will be pushing residents to keep up their medical skills to do monitoring. If we only train psychiatrists to do blood pressure monitoring alone, it would make a big difference,” said Dr. Katon, professor of psychiatry and behavioral sciences at the University of Washington in Seattle.

This dual comorbidity puts patients at increased risk for earlier mortality.

Major depression predicts an increased likelihood of cigarette smoking during adolescence (and more difficulty quitting), a sedentary lifestyle, and obesity. Patients with major depression also can feature decreased insulin sensitivity, increased inflammatory markers, and high cortisol levels, which all become risk factors for diabetes and heart disease.

“You can see why you would be at higher risk of earlier mortality,” Dr. Katon said.

Diabetes and depression are independent risk factors for dementia, based on the findings in a prospective study of 3,837 primary care patients (*J. Gen. Intern. Med.* 2010;25:423-9). “It looks like these are particularly bad conditions to have together in terms of risk of dementia,” he said.

Dr. Katon and his colleagues found that 7.9% of patients with diabetes and major depression developed dementia over a 5-year period (based on ICD-9 codes) compared with 4.8% of those with diabetes alone (fully adjusted hazard ratio, 2.69). “This was not explained by depression being a prodrome for dementia,” he said.

A more than twofold increased risk for dementia is “especially frighten-

ing,” Dr. Katon added. “It speaks to the importance of more aggressively screening diabetics for depression and more effectively treating them.”

Beyond having an increased risk of mortality and dementia, people with diabetes and depression also have lower levels of self-care, do not exercise as much, and are not as adherent to medications, compared with nondepressed diabetics (*Diabetes Care* 2004;27:2154-60).

In this study, those with diabetes and major depression had significantly more nonadherent medication days over time, compared with nondepressed diabetics. “This does not portend well for increased risk of morbidity and mortality,” Dr. Katon said.

Session moderator Dr. Herbert Pardes commented, “This is a big deal. The comorbidity of depression with a major medical condition ... people have got to pay attention to the medical health as part of the comorbidities.” Dr. Pardes is president and CEO of the New York Presbyterian Hospital in New York City.

The baseline severity of diabetes (higher number of symptoms) was a strong predictor of a patient having major depression in a 5-year follow-up study (*Psychosomatics* 2009;50:570-9).

Dr. Katon and his coauthors also found having one or more coronary procedures during the 5 years predicted major depression in this prospective study of 2,759 primary care patients with diabetes.

The study also revealed a higher likelihood for all-cause mortality associated with depression (hazard ratio, 1.53, vs. 1.23 for those without depression). “Diabetics with major depression were about 50% more likely to die than nondepressed diabetics over 5 years,” Dr. Katon said.

After confounders, including cigarette smoking and a sedentary lifestyle were controlled for, major depression was associated with more microvascular complications (HR, 1.33 vs. 1.05); more macrovascular complications (1.38 vs. 1.32), and a higher prevalence of foot ulcers (1.99 vs. 1.22).

Diabetes, depression, and coronary artery disease appear to be one of the “natural clusters of illnesses that doctors see,” Dr. Katon said. These illnesses each have a high prevalence, high comorbidity, and bidirectional adverse interactions.

Depression, chronic pain, and substance abuse comprise another natural cluster, he added “but that is a whole other lecture for another day.”

Dr. Katon said he has received honoraria from Forest Laboratories, Lilly, Pfizer, and Wyeth. ■

# Diabetes and Hypertension Tied to Risk of Brain Infarcts

BY DENISE NAPOLI

FROM NEUROLOGY

Diabetes and hypertension were strongly and independently associated with brain infarcts, as well as with atrophic changes such as increasing ventricular size and sulcal widening.

The finding, from one of the first longitudinal imaging studies to look at vascular risk factors and infarct, confirms that “control of blood sugar and blood pressure in midlife should reduce the likelihood of ischemic and atrophic changes in the brain in subsequent decades,” wrote Dr. David S. Knopman and his colleagues (*Neurology* 2011 May 4 [doi:10.1212/WNL.0b013e31821d753f]).

Dr. Knopman of the Mayo Clinic,

total cohort studied, they added.

Among the high-risk group, incident infarcts were seen in 32.6%, compared with 15.1% in the low vascular risk group, and 20.1% in the overall cohort. The risk increased with disease severity, the authors found.

“Those in the highest tertile for both fasting blood sugar and systolic blood pressure had 3.68 higher risk (95% confidence interval, 1.89-7.19) of new infarcts compared with subjects in the lowest tertile for both conditions,” they added.

Diabetes alone was also associated with incident infarct, independent of hypertension. After adjustment for variables including age, sex, race, hypertension, and prevalent stroke, diabetes conferred a nearly two-fold risk of incident infarct, compared with those patients without the condition (odds ratio, 1.96; 95% CI, 1.23-3.10).

Similarly, hypertension alone was associated with an OR for incident infarct of 1.58, compared with those patients with normal blood pressure (95% CI, 1.08-2.30).

Looking at brain atrophic changes, Dr. Knopman found that most patients had a change in ventricular size, sulcal widening, and white matter hyperintensities over the 10-year period, and older age by itself accounted for worsening in these categories.

Vascular risk factors also played a role, as 84.7% of patients in the high risk group, versus 73.2% in the low risk group, had ventricular size progression of one grade or more over the study period.

Similarly, 76.5% of high risk patients versus 55.5% in the low-risk group showed white matter hyperintensity progression. And 80.0% of high-risk patients, versus 69.6% in the low-risk group, showed an increase in sulcal widening.

The authors found no race- or sex-specific interactions between changes in brain imaging and vascular risk factors.

The study’s strengths include its large sample size, biracial composition, extensive risk factor assessment at baseline, and decade-long follow-up, the researchers said. Its weaknesses included the fact that many subjects were lost over the 10 years of follow-up. But “those persons who had follow-up scans were healthier in all respects including lower burdens of vascular risk factors, and less pathology on imaging,” they wrote.

Consequently, “our findings probably understate the links between diabetes and hypertension.”

In addition, at the time of the initial scans, volumetric MRI was not yet available, making measurement over time of that particular parameter impossible, they noted. ■

## VITALS

**Major Finding:** Over 10 years of follow-up, 32.6% of patients with hypertension and diabetes recorded a brain infarct, compared with 15.1% of those without either condition.

**Data Source:** The Atherosclerosis Risk in Communities (ARIC) Study.

**Disclosures:** Lead author Dr. Knopman disclosed being a deputy editor of *Neurology*, the journal in which this study was published. He disclosed relationships with Eli Lilly, the Elan Corporation, Baxter International, and Forest Laboratories. Additionally, he and several other investigators stated they have received grants from the National Institutes of Health and the National Heart, Lung, and Blood Institute, which partially funded the ARIC study.

Rochester, Minn., and his colleagues looked at an initially middle-aged cohort of patients from the Atherosclerosis Risk in Communities (ARIC) study, which in 1987 recruited nearly 16,000 adults aged 45-64 years from Forsyth County, N.C.; Jackson, Miss.; selected suburbs of Minneapolis; and Washington County, Md. The subset for the current study included 1,812 patients who underwent brain MRI in 1994-1995. They were 55 years and older at this time, and came from Forsyth County or Jackson.

Ten years later, between 2004 and 2006, the patients were invited to undergo a follow-up MRI and vascular health assessments. Overall, 1,112 of these follow-up images were of sufficient quality for inclusion in the present study (689 females; mean age 61.7 years).

“Compared with current participants, those who died, were ineligible, or refused to participate in the follow-up scan were older, had a much higher stroke rate, had a higher rate of diabetes and hypertension, and had worse imaging at the baseline scan,” wrote the authors.

At baseline, 50.3% of the included subjects had neither hypertension nor diabetes. These patients were classified as having “low vascular risk,” the researchers wrote. Patients with both conditions were referred to as “high vascular risk” and made up 9.2% of the