Middle-Aged Obesity Linked To Greater Risk of Dementia

People who are obese or overweight at middle age are at significantly greater risk for dementia in later life than normal-weight people, reported Rachel A. Whitmer, Ph.D., of the division of research, Kaiser Permanente, Oakland, Calif., and colleagues.

The investigators prospectively followed 10,276 people enrolled in the Kaiser Permanente medical program of northern California who were 40–45 years old between 1964 and 1973. At midlife, 10% were obese (BMI of 30 kg/m² or greater), 36% overweight (BMI 25–29.9 kg/m²), and 53% normal weight (BMI 18.6–24.9 kg/m²).

From January 1994 to April 2003, people who were obese at midlife had a 74% greater risk of dementia, compared with people who had been of normal weight, while overweight people had a 35% greater risk.

In women, the corresponding increases were 107% for obesity and 55% for overweight, no significant differences were found in men.

People in the highest quintile of subscapular skinfold had midlife had a 72% increased risk of dementia, while people in the highest quintile of triceps skinfold had a 59% increased risk of dementia, compared with people in the lowest fifth of the two measures. Dr. Whitmer reported in the April 29 online edition of the British Medical Journal.

Low Plasma β-Amyloid Levels May Be a Marker for Cognitive Decline

Washington — Plasma levels of β-amyloid may be low in elderly patients at risk for mild cognitive impairment or even Alzheimer’s disease in the near term, according to research presented at an international conference sponsored by the Alzheimer’s Association.

β-Amyloid is secreted as 40–42 amino acid species (A40) and a 42-amino acid species (A42), both of which are found in the blood and cerebrospinal fluid (CSF). While A40 is the most prevalent species, A42 forms the plaques that are one of the pathological hallmarks of Alzheimer’s disease (AD).

“Our results in this study indicate that the ratio of these two proteins [A42:A40] is a good biomarker for identifying those very early, with repeated measures. In the next 3–5 years,” said Neill Graff-Radford, M.D., a professor of neurology at the Mayo Clinic in Jacksonville, Fla.

The researchers followed 565 cognitively normal individuals (median age 78 years; 62% female) yearly using the Mattis Depression and Stroke/Alzheimer’s Association Rating Scale (DRS). Participants were followed for 2–12 years (median 3.7 years) after baseline plasma A42 and A40 levels were measured.

Over the course of the study, 54 individuals converted to AD or amnestic mild cognitive impairment (MCI), as diagnosed using the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer’s Association and Mayo criteria.

The researchers compared baseline A42:A40 ratios in subjects who developed AD or MCI with those who did not, after adjusting for age and apolipoprotein E genotype—two risk factors for AD. They found that subjects with A42:A40 ratios in the lowest quartile had three times the risk of developing MCI or AD, compared with those in the highest quartile.

Subjects with the lowest ratios of A42:A40 also were significantly more likely to show decline on DRS, even after adjustment for age and apolipoprotein E genotype.

Those with ratios in the lowest quartile developed AD or MCI earlier than those in the other groups, too. Participants in the lowest quartile started developing AD or MCI around 2 years’ later, while those with ratios in the next lowest quartile began around 4 years, and those in the upper half began at 6.8 years.

In those older than 80 years and with ratios in the lower half, 20% developed AD in 5 years, compared with 5% of those in the upper half.

“We have pretty convincing evidence and many of us believe that A42:A40 is a very important therapeutic target,” Dr. Graff-Radford said.

High plasma levels of A42:A40 have been associated with the early-onset genetic form of AD, Down syndrome, the aging process, and with being a relative of someone with AD. However, low A42:A40 levels have been found in the cerebrospinal fluid of patients with MCI or AD. Data from animal models suggest that low plasma and CSF levels may be a consequence of Aβ42 deposition in the brain.

A biomarker for the disease could spur research into drugs and other preventive measures.

“To develop preventive therapies for Alzheimer’s...it’s essential to have biomarkers related to Alzheimer’s that identify the people at risk,” Dr. Graff-Radford said.

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