

High Blood Pressure and High Cholesterol: Risk Factors for Alzheimer's Disease

Kivipelto M, Helkala EL, Laakso MP, et al. Midlife vascular risk factors and Alzheimer's disease in later life: longitudinal, population based study. *BMJ* 2001;322:1447-51.

Study Overview

Objective. To examine the relationship between elevated blood pressure and serum cholesterol concentrations in midlife and Alzheimer's disease in later life.

Design. Observational, prospective population-based cohort study.

Setting and participants. Participants were derived from 4 independent samples previously examined within the framework of the North Karelia project and the FINMONICA study in 1972, 1977, 1982, and 1987 [1]. Subjects who were still alive, aged 65 to 79 years by the end of 1997, and living in 2 geographically defined areas in eastern Finland were the target of the current study. From an eligible population of 2293 individuals, 2000 were randomly selected and 1449 agreed to participate in the 1998 re-examination. Mean length of follow-up was 21 years (range, 11 to 26 years).

Data collection. The original protocol for midlife examination [1] included a self-administered questionnaire on medical history, cerebrovascular and cardiovascular events, and vascular conditions diagnosed by a physician. Blood pressure was measured in the right arm after participants had been seated for 5 minutes. During the 1998 re-examination, dementia was diagnosed in a 3-phase study design: a screening phase (phase 1), a clinical phase (phase 2), and a differential diagnosis phase (phase 3). The diagnosis of dementia was based on the *Diagnostic and Statistical Manual of Mental Disorders IV*, and the diagnosis of Alzheimer's disease was made according to criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer Disease and Related Disorders Association [2].

Main outcome measures. Midlife blood pressure and cholesterol concentrations and development of Alzheimer's disease in later life.

Main results. Study participants (62% of whom were women) had a mean age of 50.4 years (range, 40 to 64 years) in the

original survey and 71.3 years (range, 65 to 80 years) in the re-examination. Of the 57 subjects who developed dementia, 48 fulfilled diagnostic criteria for probable or possible Alzheimer's disease. Individuals with an elevated systolic blood pressure (160 mm Hg or higher) or high serum cholesterol concentration (6.5 mmol/L or higher) in midlife had a significantly higher risk for later-life Alzheimer's disease than those with normal systolic blood pressure (odds ratio [OR], 2.3 [95% confidence interval {CI}, 1.0 to 5.5]) or serum cholesterol (OR, 2.1 [95% CI, 1.0 to 4.4]). This association did not change after adjustment for age, body mass index, education, vascular events, smoking status, and alcohol consumption. Participants with both risk factors in midlife had a significantly higher risk of developing Alzheimer's disease than those with either risk factor alone (OR, 3.5 [95% CI, 1.6 to 7.9]). Midlife diastolic blood pressure had no significant effect on Alzheimer's disease risk.

Conclusion. Elevated systolic blood pressure and high serum cholesterol concentration in midlife increase risk for Alzheimer's disease in later life. The combination of these factors particularly increases risk.

Commentary

Alzheimer's dementia is a common problem in the elderly population, with devastating consequences for patients and caregivers. Research has focused on developing therapies, especially drugs, that will reverse cognitive impairment and improve prognosis (5- to 10-year survival after diagnosis). Although available treatments seem to improve cognitive function, their long-term effects on the disease are uncertain. Identifying modifiable risk factors will open another battlefield in the fight against this debilitating disease and ideally should produce the best outcome—primary prevention.

Data provided by this study have the advantage of a population-based prospective source but are limited to whites. Interestingly, although it represents an important risk factor for vascular disease in general, elevated diastolic blood pressure in midlife did not increase risk for

Alzheimer's disease. Further research is needed to identify other risk factors and to evaluate if their modification decreases risk of developing Alzheimer's disease later in life.

Applications for Clinical Practice

The efforts invested in screening and managing risks factors for atherosclerosis might also be beneficial in preventing not only vascular dementia but also Alzheimer's disease.

References

1. Vartiainen E, Puska P, Jousilahti P, et al. Twenty-year trends in coronary risk factors in north Karelia and in other areas of Finland. *Int J Epidemiol* 1994;23:495-504.
2. McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of the Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984;34:939-44.

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