

Hypertension and cognitive impairment

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Numerous studies have demonstrated that hypertension increases the risk for cognitive impairment, vascular dementia, and Alzheimer's disease (1-11). In a 5-year longitudinal study of 353 community-dwelling persons, mean age 72 years, increased blood pressure variability was associated with poorer cognitive function (5). In a study of 1,373 persons aged 59 to 71 years of age in France, the risk of cognitive impairment at 4-year assessment was increased 2.8 times in persons with hypertension (2). In persons with hypertension, the risk of cognitive impairment was increased 4.3 times in persons who were not treated with antihypertensive drug therapy versus increased 1.9 times in persons treated with antihypertensive drug therapy (2). In a study of 1,301 persons aged 75 years and older without dementia, at 3-year mean follow-up, persons with hypertension treated with antihypertensive drug therapy had a 30% lower incidence of dementia than persons with hypertension not treated with antihypertensive drug therapy (1).

In 7,046 elderly persons free of dementia at baseline in the Rotterdam Study, at a mean follow-up of 2.2 years, persons taking antihypertensive drug therapy at baseline had a 24% reduced incidence of dementia (11). This risk decrease was 30% for vascular dementia and 13% for Alzheimer's disease (11). In a prospective study of 6,426 women aged 65 to 79 years with intact cognition in the Women's Health Initiative Memory Study, at 9.1-year median follow-up, the presence of hypertension increased the risk for cognitive impairment 20% (10). Women with a blood pressure of 140/90 mmHg or higher despite antihypertensive drug therapy had a 30% increased risk of developing cognitive impairment (10). Dietary sodium intake did not modify the increased risk for cognitive impairment in the women with hypertension taking

antihypertensive drug therapy (10).

Hypertension is the main risk factor for the development of ischemic white matter lesions in the brain (12). Cranial magnetic resonance images were obtained in a study of 3,301 persons aged 65 years and older without a history of stroke or transient cerebral ischemic attack in the Cardiovascular Health study (13). Hypertension was one of the risk factors significantly associated with the presence of white matter lesions which are associated with impaired cognitive function (13). Cerebral magnetic resonance images were also obtained in 1,920 persons aged 55 to 72 years in the Atherosclerosis Risk in communities Study (14). Compared to persons without hypertension, white matter lesions grade 3 and higher were 2.34 times increased in all persons with hypertension and 3.40 times increased in persons with treated uncontrolled hypertension (14).

Numerous randomized, double-blind, placebo-controlled trials have demonstrated that antihypertensive drug therapy reduces cardiovascular events including stroke and mortality in older persons (15). Reduction of stroke will reduce the incidence of vascular dementia. Treatment of hypertension may reduce vascular dementia and Alzheimer's disease (6). However, the data from randomized, controlled clinical trials for antihypertensive drug treatment preventing dementia are conflicting (6).

The new guidelines for treatment of patients with hypertension will be strongly influenced by the results from the Systolic Blood Pressure Intervention Trial (SPRINT) (16,17). SPRINT randomized 9,361 patients with a systolic blood pressure of 130–180 mmHg and an increased cardiovascular risk to a systolic blood pressure of less than 120 mmHg or to less than 140 mmHg. Median follow-up was 3.26 years for all persons (16) and 3.14 years in the group aged 75 years and older (17).

The primary composite outcome was myocardial infarction, other acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes and was decreased 25% by intensive blood pressure treatment in the entire group (16) and by 34% in persons aged 75 years and older (17). All-cause mortality was decreased by 27% by intensive blood pressure treatment in the entire group (16) and by 33% in persons aged 75 years and older (17). The persons in this study aged 75 years and older are being followed at present to determine the effect of lowering the systolic blood pressure to less than 140 mmHg versus less than 120 mmHg on cognitive function.

Randomized, controlled clinical trial data on the efficacy of antihypertensive drug treatment on prevention of dementia are conflicting (18-23). The Systolic Hypertension in the Elderly Program randomized 4,736 persons aged 60 years and older with isolated systolic hypertension to antihypertensive drug therapy versus double-blind placebo (18). Mean follow-up was 5 years. Compared to placebo, antihypertensive drug therapy insignificantly reduced cognitive impairment (18). The Systolic Hypertension in Europe (SYST-EUR) trial randomized 2,418 persons aged 60 years and older with isolated systolic hypertension to antihypertensive drug therapy versus double-blind placebo (19). Median follow-up was 2.0 years. This study showed that compared to placebo, antihypertensive drug therapy significantly reduced the incidence of dementia by 50% (19). The extended follow-up to 3.9 years of the SYST-EUR trial showed that compared with the control group, antihypertensive drug therapy significantly reduced the incidence of dementia by 55% (20).

The Perindopril Protection Against Recurrent Stroke Study (PROGRESS) randomized 6,105 persons with a prior stroke or transient ischemic attack to perindopril or perindopril plus indapamide versus double-blind placebo (21). At a mean follow-up of 3.9 years, compared with placebo, drug therapy insignificantly reduced the incidence of dementia by 12% and significantly reduced the incidence of cognitive decline by 19% (21). The Hypertension in the Very Elderly Trial randomized 3,336 persons aged 80 years and older with hypertension to treatment with antihypertensive drug therapy versus double-blind placebo (22). At 2-year follow-up, compared with placebo, antihypertensive drug therapy insignificantly reduced the incidence of dementia by 14% (22). However when these data were combined in a meta-analysis with three other studies discussed in this paper (18,19,21), antihypertensive drug therapy significantly reduced the

incidence of dementia by 13% (22).

The Heart Outcomes Prevention Evaluation (HOPE) Study randomized 9,297 patients aged 55 years and older with vascular disease or diabetes mellitus plus an additional risk factor to ramipril versus double-blind placebo (23). Follow-up was 4.5 years. Compared to placebo, ramipril significantly reduced the incidence of stroke by 32% and the incidence of cognitive impairment by 41% (23).

We can conclude from the available data that hypertension is associated with dementia and cognitive impairment. Observational data support the reduction of dementia and cognitive impairment by antihypertensive drug therapy. We can also conclude that despite the short follow-up of the double-blind antihypertensive drug versus placebo trials on the incidence of dementia and cognitive impairment, the data show that antihypertensive drug therapy either significantly reduces the incidence of dementia or of cognitive impairment (three trials) or insignificantly reduces the incidence of dementia or cognitive impairment (two trials) with a meta-analysis of four trials (18,19,21,22) showing that antihypertensive drug therapy significantly reduces the incidence of dementia. Data are needed to show which antihypertensive drugs best reduce the incidence of dementia and cognitive impairment. Data are also needed to know what the blood pressure treatment goal should be to optimally reduce dementia and cognitive impairment. Data from the ongoing SPRINT trial when available will tell us how lowering the systolic blood pressure to less than 120 mmHg versus less than 140 mmHg in persons aged 75 years and older with hypertension affects cognitive function.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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