

## ■ Review

## Cardiovascular causes of dementia

### *Demansın kardiyovasküler sebepleri*

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#### Abstract

Dementia, as a geriatric syndrome, is an increasing concern as the ageing population grows worldwide and it is more common due to enhanced diagnostic tools. The incidence of dementia is low before 75 years of age and increases exponentially with age, even in the oldest age groups. Dementia and heart health are in close relationship. Coronary artery disease risk factors, atrial fibrillation, heart failure and some medications given for cardiovascular diseases can lead to dementia via systemic effects and also worsen dementia. Prevention and treatment of cardiovascular disease in early ages and the choice of medications may affect prognosis of dementia as well as primary cardiovascular disease.

**Keywords:** Cardiovascular; dementia; elderly

#### Öz

Geriatrik bir sendrom olan demans, dünya çapında yaşlı popülasyondaki artış ve gelişmiş tanı araçları sebebiyle giderek artan bir sağlık problemidir. Demans insidansı 75 yaşından önce düşüktür ve ileri yaş gruplarında bile yaşla birlikte katlanarak artmaktadır. Demans ve kalp sağlığı yakın ilişki içindedir. Koroner arter hastalığı risk faktörleri, atriyal fibrilasyon, kalp yetmezliği ve kardiyovasküler hastalıklar için verilen bazı ilaçlar sistemik etkiler ile demansa neden olabilir ve demansı kötüleştirebilir. Erken yaşta kardiyovasküler hastalıkların önlenmesi ve tedavisi için uygun ilaç seçimi primer kardiyovasküler hastalığın yanı sıra demans prognozunu etkileyebilir.

**Anahtar kelimeler:** Kardiyovasküler; demans; yaşlı

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## Introduction

Dementia, as a geriatric syndrome, is an overall term for a set of symptoms that are caused by disorders affecting the brain. Symptoms may include memory loss and difficulties with thinking, problem-solving or language, severe enough to reduce a person's ability to perform everyday activities. A person with dementia may also experience changes in mood or behavior[1]. Dementia is not a specific disease. Many diseases can cause dementia, including Alzheimer's disease, vascular dementia (due to strokes), Lewy Body disease, head trauma, fronto-temporal dementia, Creutzfeldt-Jakob disease, Parkinson's disease, and Huntington's disease. These conditions can have similar and overlapping symptoms. Some treatable conditions can produce symptoms similar to dementia, for example, vitamin deficiencies, thyroid disease, sleep disorders, or mental illness. It is therefore important to arrange for a full medical assessment as early as possible[2]. Dementia is an increasing concern as the ageing population grows worldwide and it is more common due to enhanced diagnostic tools. The incidence of dementia is low before 75 years of age and increases exponentially with age, even in the oldest age groups[3]. Amyloid accumulation eventually leading to AD neurodegeneration starts decades before clinical symptoms emerge like atherosclerosis process starts early in adulthood[4].

Vascular risk factors associated with dementia and cognitive impairment include hypertension, hypercholesterolemia, diabetes, obesity and smoking. It is controversial whether or not some of these factors have a direct impact on the development of the specific neuropathological lesions in Alzheimer's disease(AD) or if the effects are mediated by cerebrovascular disease or both. Importantly, these vascular risk factors are modifiable, representing an opportunity for interventions that could prevent or postpone the onset of dementia with a possible major effect on public health[5,6].

## Hypertension

Arterial hypertension is an important risk factor for the development of cerebrovascular events. The basal measurements of the middle age group were found to be at risk for the development of vascular dementia in the long-term follow-up of individuals who were compatible with hypertension[7,8]. Studies have shown that high systolic blood pressure is a significant risk factor for the development of vascular dementia[8,9]. In Honolulu Asia Aging Study patients were followed up for 25 years and at the end of this study it is found that 27% of dementia syndromes depends on

untreated hypertension[9]. In another study, including 1385 patients with mild cognitive disorder, after 2 years of follow-up, hypertensive patients with high systolic blood pressure were found to have faster cognitive deterioration and a significant deterioration in visual-motor abilities[10]. In addition to the fact that middle age hypertension is known as a definite risk factor, the results of late age hypertension studies on cognitive functions are contradictory. Optimal blood pressure value for brain functioning is important. Just like high blood pressure, too low arterial blood pressure or inappropriate treatment can disrupt the cognitive functions by disrupting brain blood flow[11]. In addition, rapid changes in blood pressure may affect cerebral blood supply. Hippocampus, the entorhinal cortex and the prefrontal cortex are the brain regions affected most by perfusion changes and also responsible for memory and executive functions[12,13]. There are also studies showing that increased pulse pressure is a risk factor for cognitive impairment and Alzheimer type dementia development[14].

Effects of hypertension treatment on dementia is also important. AHA/ASA recommends treating high blood pressure in patients who had a stroke before to prevent dementia occurrence. The same level of certainty and suggestion is not relevant for the treatment of hypertension and dementia after 80 years of age[15,16].

In patients  $\geq 80$  years of age hypertension treatment starting threshold is  $\geq 160$  mmHg and treatment target is 140-150 mmHg. In the elderly all hypertension drugs are recommended, but diuretics and calcium antagonists are preferred more frequently in isolated systolic hypertension[17].

If the average of systolic blood pressure is  $\geq 130$  mmHg treatment is recommended for the elderly ( $> 65$  years) who are able to take care of themselves and the treatment target is  $< 130$  mmHg[18]. Large population studies with longer follow-up period are needed to understand the effects of antihypertensive agents on cognition.

## Hyperlipidemia

Atherosclerosis has an important role in the development of coronary artery disease(CAD) and dementia. Often, dementia shares the same etiologic factors as CAD. In Cardiovascular health study, patients with CAD had a higher incidence of dementia[19]. Cytotoxicity and inflammation, which are also related with hypercholesterolemia has an important role in the pathophysiology of dementia. Therefore, uncontrolled cholesterol load is a triggering factor in the brain atrophy. It is shown that middle age cholesterol is an independent risk factor for dementia development[20]. In autopsy studies,

it was observed that high LDL levels in early age significantly increased amyloid load[21]. It is the focus of interest that statin use will be associated with dementia, especially Alzheimer type dementia. Since older people usually have co-morbidities and their pharmacokinetics are different, lipid-lowering therapies should be initiated with low dose and dose titrations should be performed more carefully to achieve lipid therapy targets[22].

### Heart Failure

It was understood that heart failure caused cognitive impairment and cognitive impairment progressed as the severity of the disease increased[23,24]. Mechanisms that explain the pathology and destruction are reduced neuron oxygenation, increased oxidative stress, and lack of amyloid removal. Decreased left ventricular ejection fraction and cardiac output has been associated with abnormal brain aging and impaired cognition[25,26]. It has been shown that cerebrospinal fluid decreases in patients with heart failure and this increases the frequency of cognitive impairment[27]. There is also relationship between heart failure medications and cognitive functions. Diuretic therapy which is one of the cornerstones of the treatment may effect electrolyte balance and hyponatremia may cause cognitive deterioration[28]. The correction of hyponatremia should also be managed extremely careful. Because if hyponatremia is remedied quickly, central pontine can cause irreversible brain damage by causing myelinolization.

Angiotensin 2 receptor blockers, which are frequently used in the treatment of heart failure has neuroprotective effects as a neuromuscular blocker[29].

For this reason, the side effects and protective effects of the drugs should be taken into consideration, the benefit and loss balance should be calculated and than medication should be decided. It may be better to follow old patients with heart failure in a multidisciplinary geriatric clinic including ideal rehabilitation programs.

### Atrial Fibrillation

There is growing evidence that atrial fibrillation (AF) is associated with higher risk of dementia and Alzheimer's disease[30], raising the possibility that interventions targeting AF might prevent or delay some cases of dementia.

It is very well known that atrial fibrillation causes embolic strokes and silent cerebral emboli, also it deteriorates cognitive functions by causing cerebral hypoperfusion. Possible mechanisms include embolic strokes [31], silent cerebral emboli [32], and cerebral hypoperfusion [33,34]. It is not known

whether AF contributes to AD-associated neuropathologic changes such as neurofibrillary tangles and neuritic plaques. In a study supported by postmortem examinations, infarct areas in the brain were observed to be more frequent in patients with atrial fibrillation. It has been demonstrated in large meta-analyses that AF is an independent risk factor for dementia except causing stroke[35,36].

As a result, dementia and heart health are in close relationship. Cardiovascular disease, another common health problem among elderly people can lead to dementia via systemic effects and also worsen dementia. Prevention and treatment of cardiovascular disease in early ages and the choice of medications may affect prognosis of dementia as well as primary cardiovascular disease[5].

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