v. 4, n. 95, 2024

International Journal of Health Science

Acceptance date: 25/10/2024

IMPACT OF CARDIOVASCULAR RISK FACTORS ON THE PREVENTION AND PROGRESSION OF VASCULAR DEMENTIA

Laura Garcia
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0009-2328-50492

Jackeline Delfini Ribeiro
Faculdade de Ciências Médicas de Três Rios
Três Rios – RJ
https://orcid.org/0009-0006-5513-2774

Beatriz Garcia Kobal Bezerra
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0000-6092-9346

Caio Queiroz Esprícido
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0006-6927-2137

Maria Isadora Manfio Corrêa
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0006-0091-5675

Larissa Silva Matiolli Martins
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0001-8447-2173

Ana Flávia Cardoso
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0006-5188-7010

Joyce Nunes Vieira
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0002-2914-6284

Ana Laura Mascarin
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0009-3166-5383

Thaís Nassar de Rossi
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0005-5126-1344

Maria Carolina Poli Delamuta
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0002-2733-9357

Larissa Costa de Oliveira
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0005-3351-2322

Abstract: INTRODUCTION: Dementia refers to the progressive loss of cognitive functions, which affects the ability to carry out daily activities. It results from pathological conditions, such as Vascular Dementia, which accounts for 10% to 20% of cases in the elderly. Its prevalence increases with age, especially in individuals with cardiovascular comorbidities. Vascular Dementia results from damage to the blood vessels in the brain, leading to cell death due to hypoxia. The main risk factors include hypertension, diabetes, smoking and physical inactivity. This condition compromises quality of life, generating dependency, psychological suffering and high social costs. OBJECTIVES: This study aims to analyze the impact of cardiovascular risk factors on the prevention and progression of vascular dementia, identifying the most influential ones and exploring biological mechanisms such as atherosclerosis and stroke. It also analyzes the impact of lifestyle and compares interventions, seeking to provide guidance for health professionals and the public on the prevention and treatment of vascular dementia. METHODS: This integrative review investigated the impact of cardiovascular risk factors on vascular dementia, using articles published between 2019 and 2024 in the VHL, PUBMED and MEDLINE databases, with specific keywords. The selection process involved three stages: identification of 257 articles, exclusion of 169 for irrelevant topics, resulting in 88 reviewed, of which 34 were included in the final analysis to compare approaches to prevention and management of vascular dementia. RESULTS AND DISCUSSION: Cerebrovascular diseases are important causes of cognitive impairment in the elderly, including atherosclerosis, arteriolosclerosis, cerebral amyloid angiopathy (CAA) and microvascular disease. These affect the brain in different ways, causing infarcts, hemorrhages and brain atrophy. The overlap of cerebrovascular pathologies and

Alzheimer's in the elderly makes diagnosis difficult, since factors such as hypertension, diabetes, dyslipidemia and smoking influence vascular and cerebral health. Hypertension is a risk factor for vascular dementia, damaging vessels and promoting inflammation and ischemic lesions such as leukoaraiosis. The interaction between genetic and environmental factors, such as diet and stress, influences the progression and development of dementia. Type 2 diabetes mellitus is associated with vascular dementia due to hyperglycemia and insulin resistance, which damage the endothelium and compromise cerebral vascular function. Genetic and epigenetic factors, such as diet and chronic inflammation, influence the progression of the disease. Dyslipidemia increases the risk of vascular dementia through atherosclerosis and chronic inflammation, impairing endothelial function and increasing susceptibility to brain damage. Genes related to lipid metabolism and inflammation also contribute to this risk. Adopting lifestyle changes and pharmacological treatments is crucial to controlling dyslipidemia and reducing vascular dementia. Finally, smoking has a negative impact on blood vessel health, contributing to the development and worsening of vascular dementia. CONCLUSION: Cerebrovascular diseases play a crucial role in the development of cognitive impairment and dementia, especially in the elderly, due to the overlap of vascular pathologies. Cardiovascular risk factors such as hypertension, diabetes and dyslipidemia, smoking and physical inactivity contribute significantly to vascular dementia. Understanding genetic and epigenetic interactions is essential for developing effective preventive strategies. Controlling risk factors and promoting healthy habits are key to reducing morbidity and improving the quality of life of the elderly.

Keywords: Dementia, Vascular Dementia, Cardiovascular Risk Factors, Cerebrovascular Diseases.

INTRODUCTION

Dementia is a generic term that refers to a set of symptoms related to the progressive loss of cognitive functions, which affect an individual's ability to carry out daily activities and engage in social interactions [1]. This condition is a result of various pathologies, such as Alzheimer's, Vascular Dementia, Lewy Body Dementia and other forms of cognitive deterioration and is characterized as one of the main public health challenges, especially in elderly populations [1]. Vascular Dementia, in particular, is the second most common form among dementia types, accounting for between 10% and 20% of dementia cases in the elderly [1,2]. It is estimated that Vascular Dementia is more frequent in individuals who have cardiovascular comorbidities, such as hypertension, diabetes and heart disease, reflecting the interconnection between vascular and cognitive health [1,2].

Vascular dementia affects the quality of life of the elderly in significant ways. This condition can lead to difficulties in carrying out daily activities, compromising autonomy and increasing dependence on caregivers and family members [3]. In addition, it is often accompanied by symptoms such as mood swings, depression and anxiety, exacerbating the psychological suffering of patients and their families [3]. At the same time, it is associated with high social and economic costs, both in terms of medical care and long-term support, representing a growing challenge as the elderly population continues to increase globally [4].

Vascular Dementia is a type of dementia that results from damage to the blood vessels in the brain, leading to progressive cognitive impairment. This damage can occur through small infarcts, hemorrhages or other vascular diseases that interrupt cerebral blood flow [4]. The deprivation of nerve cells of oxygen and essential nutrients causes cell death and the

consequent loss of cognitive functions. As a result, the individual can develop dementia symptoms, which vary according to the location and extent of the brain damage [4,5].

Lesions in the frontal areas, for example, can cause problems with attention, planning, judgment and impulse control, leading to changes in behavior and personality [5]. Lesions in the temporal regions affect memory, language and the ability to recognize objects and people [5]. Parietal lesions, in turn, compromise spatial perception, attention and calculation, while subcortical lesions result in slowness, rigidity, tremors and difficulties in motor coordination [5]. This complexity requires an integrated approach to diagnosis, prevention and treatment, with an emphasis on managing cardiovascular risk factors.

The risk factors for developing vascular dementia are largely associated with cardiovascular conditions, such as high blood pressure, diabetes, smoking and physical inactivity, which increase the likelihood of cerebral vascular damage [6]. Additional factors such as older age, family history, sleep apnea and atrial fibrillation also play a significant role in increasing this risk [6]. Sleep apnea can cause hypoxemia during the night, compromising blood vessels, while atrial fibrillation facilitates the formation of blood clots, increasing the risk of strokes and, consequently, brain damage associated with vascular dementia [7].

OBJECTIVES

This study aims to quantify the magnitude of the impact of cardiovascular risk factors on the prevention and progression of vascular dementia, identifying those with the greatest influence. It seeks to explore the underlying biological mechanisms, such as atherosclerosis, hypertension and inflammation, which contribute to the development of the condition, as well as identifying gaps in research to stimulate future investigations [7]. In addition, it analyzes the impact of lifestyle, smoking and compares the effectiveness of intervention models, ranging from behavioral changes to the use of medication [7]. In this way, it aims to provide applicable guidelines for both health professionals and the general population on the prevention and treatment of vascular dementia.

METHODS

This integrative review was carried out with the aim of investigating the impact of cardiovascular risk factors on the prevention and progression of vascular dementia. The searches were conducted in the Virtual Health Library (VHL), PUBMED and MEDLINE virtual databases, covering articles published between 2019 and 2024, in English. The following keywords were used: "vascular dementia", "cardiovascular risk factors", "prevention of vascular dementia", "progression of vascular dementia", and "lifestyle interventions" [7,8].

The article selection process was divided into three stages. In the first stage, 257 articles were identified. In the second stage, studies with repetitive themes, inconclusive data, experimental trials, dissertations, theses, conference abstracts and articles that did not directly address the relationship between cardiovascular risk factors and vascular dementia were excluded, resulting in 88 articles. In the final stage, these 88 articles were fully reviewed, leading to the inclusion of 34 studies in the final analysis, after excluding publications with redundant, inconclusive results or low clinical relevance. From this refined selection, the extracted data was organized and analyzed to construct the review and compare the approaches related to the prevention and management of vascular dementia according to cardiovascular risk factors [7,8].

RESULTS AND DISCUSSION

Cerebrovascular diseases play a significant role in dementia-related cognitive impairment, especially among the elderly. Among the main types, Atherosclerosis, Arteriolosclerosis, Cerebral Amyloid Angiopathy (CAA) and Microvascular Disease are frequently observed and have specific characteristics that make them harmful to the brain [7,8]. Atherosclerosis affects the lining of the large arteries and can lead to infarcts that affect both the gray and white matter. Arteriolosclerosis, on the other hand, affects small arterioles, resulting in lacunar infarcts and microhemorrhages that can contribute to cognitive deficits [8]. CAA is characterized by the accumulation of amyloid-β in blood vessels, associated with hemorrhages and cortical microinfarcts, while Microvascular Disease impairs the delivery of nutrients and the removal of metabolic waste, resulting in brain atrophy [8]. The coexistence of these conditions, as demonstrated in neuropathological studies, illustrates the complexity of the clinical picture and the challenges in diagnosing and managing vascular dementias [8,9].

Epidemiologically, the impact of these cerebrovascular diseases on the elderly is alarming. Neuropathological studies show that a significant proportion of the elderly population diagnosed with dementia have overlapping cerebrovascular and Alzheimer's diseases, making it difficult to distinguish between these conditions and increasing the associated burden of morbidity [9]. Cerebrovascular pathologies are strongly influenced by cardiovascular factors, since conditions such as hypertension, diabetes, dyslipidemia and smoking affect vascular health and cerebral perfusion [9].

The clinical picture of vascular dementia is characterized by a combination of cognitive, behavioural, motor, visual and physical symptoms [10]. Cognitive symptoms include memory impairment, attention difficulties, language problems, reasoning difficulties and disorientation [10]. Behaviorally, patients may show mood swings, personality changes and anxiety. In motor terms, slowness, stiffness and balance problems are common, increasing the risk of falls. Visual changes and difficulties in spatial perception can also occur, as well as incontinence and swallowing difficulties in more advanced stages [10,11]. The progression of the disease can be gradual or abrupt, often related to strokes, and patients often have comorbidities such as hypertension, diabetes and heart disease, which make clinical management difficult [11].

HYPERTENSION

Hypertension acts as a significant risk factor for vascular dementia through mechanisms involving vascular damage, brain lesions and inflammation, with the contribution of genetic and epigenetic factors that modulate this relationship [11,12]. Proper blood pressure management and the modification of associated risk factors are fundamental for the prevention of vascular dementia and its cognitive complications [13].

Chronic hypertension plays a crucial role in the pathogenesis of vascular dementia through various mechanisms. Firstly, it causes damage to blood vessels by generating stress on their walls, promoting atherosclerosis and hardening of the vessels, which results in reduced cerebral blood flow and the occurrence of ischemic lesions, such as small infarcts [13]. In addition, hypertension can lead to leukoaraiosis, characterized by the demyelination and death of neurons in the subcortical areas of the brain, compromising the neural networks responsible for cognition [14]. Another important effect of hypertension is the increased permeability of the blood-brain barrier, allowing the entry

of harmful and inflammatory substances that damage neurons and glial cells [14,15]. Finally, hypertension is associated with a chronic inflammatory state, which can induce direct neuronal damage and trigger neurodegenerative processes, accelerating cognitive decline and contributing to the progression of vascular dementia [16].

Hypertension is influenced by a complex interaction of genetic factors, including components such as the Renin-Angiotensin-Aldosterone System (RAAS), calcium channels and the autonomic nervous system [16]. Genes that encode elements of the RAAS, such as the angiotensin II receptor (AGTR1) and the angiotensin-converting enzyme (ACE), are strongly associated with hypertension; genetic variations in these genes can increase sensitivity to the RAAS, resulting in significant elevations in blood pressure. In addition, the SCN5A gene, which encodes calcium channels, plays an essential role in regulating vascular tone and cardiac muscle contraction; mutations in this gene can contribute to the development of hypertension [16]. Finally, genes that regulate the sympathetic nervous system are also implicated in hypertension, where genetic variations can increase sympathetic activity and consequently raise blood pressure. These genetic factors, combined, help to explain individual predisposition to hypertension and its implications for vascular health.

However, gene expression is influenced by environmental factors such as diet, lifestyle, stress and exposure to toxins. The interaction between genes and the environment is complex and largely determines an individual's risk of developing hypertension and vascular dementia [16]. In this respect, epigenetics, which refers to hereditary modifications in gene expression that do not involve changes in the DNA sequence, is largely triggered by environmental factors such as diet, stress and a sedentary lifestyle [16,17].

In this sense, hypertension can be influenced by epigenetic factors such as DNA methylation and histone modifications [18]. These factors can be triggered by external elements, such as a diet rich in carbohydrates and saturated fats, stress and a sedentary lifestyle. Throughout life, these factors accumulate and may be closely associated with the development of vascular dementia in older people [18]. The resulting epigenetic modifications can affect the expression of genes related to cardiovascular function, inflammation and cell death. In addition, these changes can impact neuroplasticity and the response to oxidative stress, which are crucial for brain health [18].

DIABETES MELLITUS 2

Diabetes mellitus, especially type 2, is strongly associated with the development of vascular dementia through a combination of metabolic and vascular factors. The chronic increase in blood glucose levels can lead to hyperglycemia, which is related to endothelial damage and inflammation, resulting in atherosclerosis and reduced cerebral blood flow [19]. This can cause ischemic lesions, including small infarcts, which affect brain structures involved in cognitive functions [19].

In addition, diabetes can cause a state of insulin resistance, which not only impairs glucose metabolism, but also affects the regulation of vascular tone and homeostasis. Insulin resistance is associated with an increase in the permeability of the blood-brain barrier, allowing harmful substances to enter the brain and contributing to cell death [20]. Patients with diabetes are also at greater risk of developing leukoaraiosis, a condition that results from the death of neurons and demyelination in the subcortical areas of the brain, leading to cognitive impairment [20].

With regard to genetics, several genetic variants are associated with diabetes and the risk of vascular dementia. Genes related to glucose metabolism, insulin regulation and endothelial function, such as the TCF7L2 gene, are implicated in the predisposition to type 2 diabetes [21]. In addition, polymorphisms in genes that affect inflammation and the response to oxidative stress may increase the risk of cerebrovascular complications in diabetic individuals [21].

Environmental factors can have a major impact on the patient's clinical condition. Diets rich in sugars and fats can induce epigenetic changes that affect the expression of genes involved in inflammation, endothelial function and insulin resistance, exacerbating the risk of brain damage [22]. Chronic activation of the transcription factor NF-κB is associated with low-grade inflammation, which can damage vascular integrity and contribute to cognitive deterioration, since chronic inflammation damages blood vessels and brain cells [22]. Pro-inflammatory cytokines such as TNF-α, IL-6 and IL-1β are of particular concern, as they promote this inflammatory process and can lead to endothelial damage, increasing the risk of cerebrovascular disease. Endothelial function is equally crucial, with the enzyme eNOS, which produces nitric oxide essential for vasodilation, being impaired in high-fat diets. This can result in reduced cerebral blood flow and conditions such as atherosclerosis, contributing to vascular dementia [22,23].

DYSLIPIDEMIA

Dyslipidemia, characterized by abnormal levels of lipids in the blood, is a significant risk factor for the development of vascular dementia. This condition is associated with alterations in lipid metabolism, inflammation and vascular damage, as well as being influenced by genetic and epigenetic factors that can aggravate these processes [24]. High levels of low-density lipoproteins (LDL) and total cholesterol, for example, contribute to the formation of atherosclerotic plaques in the arteries, which can narrow and obstruct blood vessels, impairing cerebral blood flow. This obstruction results in ischemia and brain damage, leading to vascular dementia [24,25].

In addition to atherosclerosis, dyslipidemia compromises endothelial function, which is essential for vascular health. A reduction in the production of nitric oxide (NO), a crucial molecule for vasodilation, occurs as a result of dyslipidemia, which aggravates inflammation and oxidative stress [26]. These factors damage vascular and neuronal cells, increasing susceptibility to brain damage. The presence of excess lipids, especially oxidized lipoproteins, triggers a chronic inflammatory response, with the release of inflammatory cytokines such as TNF-α and IL-6, which damage neurons and promote cell death, contributing to the progression of vascular dementia [26,27].

Genetic association plays an important role in predisposition to dyslipidemia and vascular dementia. Genetic variations in genes that regulate lipid metabolism, such as the low-density lipoprotein receptor (LDLR), can predispose individuals to high cholesterol levels [27]. In addition, polymorphisms in genes that influence the inflammatory response, such as NF-κB, can amplify inflammation in dyslipidemic individuals, exacerbating vascular and neuronal damage. These genetic predispositions, in combination with epigenetic factors such as modifications in DNA me-

thylation induced by high-fat diets, influence the severity of dyslipidemia and its relationship with vascular dementia [27].

In short, dyslipidemia plays a crucial role in the pathogenesis of vascular dementia, operating through complex mechanisms involving atherosclerosis, inflammation and endothelial dysfunction [27]. The interaction with other risk factors, such as hypertension and diabetes, and the influence of epigenetic factors further increase this relationship. Adopting lifestyle changes and pharmacological treatment are essential for controlling dyslipidemia and, consequently, reducing the risk of vascular dementia [27,28]. Understanding these mechanisms is fundamental to developing effective prevention and treatment strategies, enabling more appropriate management for populations at risk [27,28].

SMOKING

The specific mechanisms by which smoking contributes to vascular dementia are complex and multifactorial. One of the main factors is the reduction in cerebral blood flow caused by the presence of carbon monoxide in cigarette smoke, which binds to hemoglobin and reduces the blood's ability to transport oxygen to the brain [29]. This chronic hypoxia can result in neuronal death and, consequently, the development of dementia. In addition, smoking increases blood viscosity, hindering circulation and increasing the risk of clots forming which can obstruct brain vessels [29]. Other substances in cigarettes cause direct damage to neurons, accelerating the process of neurodegeneration, while the alteration of the intestinal microbiota caused by smoking can affect the production of neurotransmitters and increase the permeability of the blood-brain barrier, contributing to brain inflammation [29].

In addition to the direct mechanisms, smoking interacts with other risk factors, such as apolipoprotein E (ApoE) and homocysteine. The ApoE ε4 variant, which is associated with the risk of Alzheimer's disease, further increases the vulnerability of smokers to developing dementia [30]. Similarly, smoking raises levels of homocysteine, an amino acid linked to an increased risk of cardiovascular and neurodegenerative diseases. The impact of passive smoking should also be considered, as exposure to second-hand smoke, albeit to a lesser degree, increases the risk of vascular dementia, with potentially long-lasting effects on the brain development of children and adolescents [30]. Therefore, smoking cessation is the most effective measure to reduce this risk, complemented by nicotine replacement therapies and the treatment of associated comorbidities such as hypertension and diabetes. Understanding these factors is fundamental for the prevention and management of vascular dementia, promoting brain health throughout life [30].

CONCLUSION

Cerebrovascular diseases are a critical factor in dementia-related cognitive impairment, especially among the elderly, where overlapping pathologies such as atherosclerosis, arteriolosclerosis, cerebral amyloid angiopathy and microvascular disease can aggravate the clinical situation. The impact of these conditions is alarming, as they are often associated with cardiovascular risk factors such as hypertension, diabetes and dyslipidemia, which contribute significantly to the development and progression of vascular dementia [31,32].

The clinical picture, characterized by a diversity of cognitive, behavioural and physical symptoms, represents a challenge in diagnosis and management, with hypertension being one of the main intervening factors which,

through multiple mechanisms, triggers vascular damage and neurodegeneration. In addition, genetic and epigenetic interactions shape individual predisposition, highlighting the importance of prevention and intervention strategies that address these risk factors [33].

In short, recognizing the complexity of cerebrovascular diseases and their multiple determinants is essential for developing effective approaches aimed at promoting brain health and minimizing the risks of vascular dementia. The appropriate management of risk factors and the promotion of healthy lifestyles are fundamental to reducing the burden of morbidity associated with these conditions and improving the quality of life of the elderly population [33,34].

REFERENCES

1. Dang C, Wang Q, Zhuang Y, Li Q, Feng L, Xiong Y, Lu Y. Pharmacological treatments for vascular dementia: a systematic review and Bayesian network meta-analysis. Front Pharmacol. 2024 Aug 22;15:1451032. doi: 10.3389/fphar.2024.1451032. PMID: 39239652; PMCID: PMC11374729.

2. McShane R, Westby MJ, Roberts E, Minakaran N, Schneider L, Farrimond LE, Maayan N, Ware J, Debarros J. Memantine for dementia. Cochrane Database Syst Rev. 2019 Mar 20;3(3):CD003154. doi: 10.1002/14651858.CD003154.pub6. PMID: 30891742; PMCID: PMC6425228.

3. Tayler HM, Skrobot OA, Baron DH, Kehoe PG, Miners JS. Dysregulation of the renin-angiotensin system in vascular dementia. Brain Pathol. 2024 Jul;34(4):e13251. doi: 10.1111/bpa.13251. Epub 2024 Mar 7. PMID: 38454306; PMCID: PMC11189771.

4. Trujillo-Rangel WÁ, Acuña-Vaca S, Padilla-Ponce DJ, García-Mercado FG, Torres-Mendoza BM, Pacheco-Moises FP, Escoto-Delgadillo M, García-Benavides L, Delgado-Lara DLC. Modulation of the Circadian Rhythm and Oxidative Stress as Molecular Targets to Improve Vascular Dementia: A Pharmacological Perspective. Int J Mol Sci. 2024 Apr 16;25(8):4401. doi: 10.3390/ijms25084401. PMID: 38673986; PMCID: PMC11050388.

5. Sokolovič L, Hofmann MJ, Mohammad N, Kukolja J. Neuropsychological differential diagnosis of Alzheimer's disease and vascular dementia: a systematic review with meta-regressions. Front Aging Neurosci. 2023 Nov 6;15:1267434. doi: 10.3389/fnagi.2023.1267434. PMID: 38020767; PMCID: PMC10657839.

6. Caruso P, Signori R, Moretti R. Small vessel disease to subcortical dementia: a dynamic model, which interfaces aging, cholinergic dysregulation and the neurovascular unit. Vasc Health Risk Manag. 2019 Aug 7;15:259-281. doi: 10.2147/VHRM.S190470. PMID: 31496716; PMCID: PMC6689673.

7. Akhter F, Persaud A, Zaokari Y, Zhao Z, Zhu D. Vascular Dementia and Underlying Sex Differences. Front Aging Neurosci. 2021 Sep 8;13:720715. doi: 10.3389/fnagi.2021.720715. PMID: 34566624; PMCID: PMC8457333.

8. Tayler H, Miners JS, Güzel Ö, MacLachlan R, Love S. Mediators of cerebral hypoperfusion and blood-brain barrier leakiness in Alzheimer's disease, vascular dementia and mixed dementia. Brain Pathol. 2021 Jul;31(4):e12935. doi: 10.1111/bpa.12935. Epub 2021 Feb 25. PMID: 33410232; PMCID: PMC8412075.

9. Yi Y, Qu Y, Lv S, Zhang G, Rong Y, Li M. Comparative efficacy and safety of non-pharmacological interventions as adjunctive treatment for vascular dementia: a systematic review and network meta-analysis. Front Neurol. 2024 Jul 12;15:1397088. doi: 10.3389/fneur.2024.1397088. PMID: 39070050; PMCID: PMC11272661.

10. Dybjer E, Kumar A, Nägga K, Engström G, Mattsson-Carlgren N, Nilsson PM, Melander O, Hansson O. Polygenic risk of type 2 diabetes is associated with incident vascular dementia: a prospective cohort study. Brain Commun. 2023 Mar 6;5(2):fcad054. doi: 10.1093/braincomms/fcad054. PMID: 37091584; PMCID: PMC10118265.

11. Nordestgaard LT, Christoffersen M, Frikke-Schmidt R. Shared Risk Factors between Dementia and Atherosclerotic Cardiovascular Disease. Int J Mol Sci. 2022 Aug 29;23(17):9777. doi: 10.3390/ijms23179777. PMID: 36077172; PMCID: PMC9456552.

12. Shim JI, Byun G, Lee JT. Long-term exposure to particulate matter and risk of Alzheimer's disease and vascular dementia in Korea: a national population-based Cohort Study. Environ Health. 2023 Apr 14;22(1):35. doi: 10.1186/s12940-023-00986-9. PMID: 37060077; PMCID: PMC10105439.

13. Zhang W, Liang J, Li C, Gao D, Ma Q, Pan Y, Wang Y, Xie W, Zheng F. Age at Diagnosis of Atrial Fibrillation and Incident Dementia. JAMA Netw Open. 2023 Nov 1;6(11):e2342744. doi: 10.1001/jamanetworkopen.2023.42744. PMID: 37938842; PMCID: PMC10632957.

14. Lee CS, Lee ML, Gibbons LE, Yanagihara RT, Blazes M, Kam JP, McCurry SM, Bowen JD, McCormick WC, Lee AY, Larson EB, Crane PK. Associations Between Retinal Artery/Vein Occlusions and Risk of Vascular Dementia. J Alzheimers Dis. 2021;81(1):245-253. doi: 10.3233/JAD-201492. PMID: 33749651; PMCID: PMC8168611.

15. Chen LJ, Sha S, Stocker H, Brenner H, Schöttker B. The associations of serum vitamin D status and vitamin D supplements use with all-cause dementia, Alzheimer's disease, and vascular dementia: a UK Biobank based prospective cohort study. Am J Clin Nutr. 2024 Apr;119(4):1052-1064. doi: 10.1016/j.ajcnut.2024.01.020. Epub 2024 Jan 29. PMID: 38296029; PMCID: PMC11007746.

16. Asby D, Boche D, Allan S, Love S, Miners JS. Systemic infection exacerbates cerebrovascular dysfunction in Alzheimer's disease. Brain. 2021 Jul 28;144(6):1869-1883. doi: 10.1093/brain/awab094. PMID: 33723589; PMCID: PMC8320299.

17. Tayler HM, MacLachlan R, Güzel Ö, Miners JS, Love S. Elevated late-life blood pressure may maintain brain oxygenation and slow amyloid-β accumulation at the expense of cerebral vascular damage. Brain Commun. 2023 Apr 4;5(2):fcad112. doi: 10.1093/braincomms/fcad112. PMID: 37113314; PMCID: PMC10128877.

18. Papanastasiou CA, Theochari CA, Zareifopoulos N, Arfaras-Melainis A, Giannakoulas G, Karamitsos TD, Palaiodimos L, Ntaios G, Avgerinos KI, Kapogiannis D, Kokkinidis DG. Atrial Fibrillation Is Associated with Cognitive Impairment, All-Cause Dementia, Vascular Dementia, and Alzheimer's Disease: a Systematic Review and Meta-Analysis. J Gen Intern Med. 2021 Oct;36(10):3122-3135. doi: 10.1007/s11606-021-06954-8. Epub 2021 Jul 9. PMID: 34244959; PMCID: PMC8481403.

19. Custodero C, Ciavarella A, Panza F, Gnocchi D, Lenato GM, Lee J, Mazzocca A, Sabbà C, Solfrizzi V. Role of inflammatory markers in the diagnosis of vascular contributions to cognitive impairment and dementia: a systematic review and meta-analysis. Geroscience. 2022 Jun;44(3):1373-1392. doi: 10.1007/s11357-022-00556-w. Epub 2022 Apr 29. PMID: 35486344; PMCID: PMC9213626.

20. Bondonno CP, Bondonno NP, Dalgaard F, Murray K, Gardener SL, Martins RN, Rainey-Smith SR, Cassidy A, Lewis JR, Croft KD, Kyrø C, Gislason G, Scalbert A, Tjønneland A, Overvad K, Hodgson JM. Flavonoid intake and incident dementia in the Danish Diet, Cancer, and Health cohort. Alzheimers Dement (N Y). 2021 May 13;7(1):e12175. doi: 10.1002/trc2.12175. PMID: 34027025; PMCID: PMC8118115.

21. Hansson O, Svensson M, Gustavsson AM, Andersson E, Yang Y, Nägga K, Hållmarker U, James S, Deierborg T. Midlife physical activity is associated with lower incidence of vascular dementia but not Alzheimer's disease. Alzheimers Res Ther. 2019 Oct 20;11(1):87. doi: 10.1186/s13195-019-0538-4. PMID: 31630687; PMCID: PMC6802179.

22. Juul Rasmussen I, Tybjærg-Hansen A, Rasmussen KL, Nordestgaard BG, Frikke-Schmidt R. Blood-brain barrier transcytosis genes, risk of dementia and stroke: a prospective cohort study of 74,754 individuals. Eur J Epidemiol. 2019 Jun;34(6):579-590. doi: 10.1007/s10654-019-00498-2. Epub 2019 Mar 4. PMID: 30830563; PMCID: PMC6497814.

23. Bao X, Kang L, Yin S, Engström G, Wang L, Xu W, Xu B, Zhang X, Zhang X. Association of MAFLD and MASLD with all-cause and cause-specific dementia: a prospective cohort study. Alzheimers Res Ther. 2024 Jun 26;16(1):136. doi: 10.1186/s13195-024-01498-5. PMID: 38926784; PMCID: PMC11201326.

24. Mur J, McCartney DL, Chasman DI, Visscher PM, Muniz-Terrera G, Cox SR, Russ TC, Marioni RE. Variation in VKORC1 Is Associated with Vascular Dementia. J Alzheimers Dis. 2021;80(3):1329-1337. doi: 10.3233/JAD-201256. PMID: 33682710; PMCID: PMC8150662.

25. Ma H, Zhou T, Li X, Heianza Y, Qi L. Use of fish oil supplements is differently related to incidence of all-cause and vascular dementia among people with the distinct APOE ε4 dosage. Clin Nutr. 2022 Mar;41(3):731-736. doi: 10.1016/j.clnu.2022.01.019. Epub 2022 Feb 3. PMID: 35172255; PMCID: PMC8897253.

26. Zhang Y, Yang H, Li S, Li WD, Wang Y. Consumption of coffee and tea and risk of developing stroke, dementia, and poststroke dementia: A cohort study in the UK Biobank. PLoS Med. 2021 Nov 16;18(11):e1003830. doi: 10.1371/journal.pmed.1003830. PMID: 34784347; PMCID: PMC8594796.

27. Yuan S, Huang X, Zhang L, Ling Y, Tan S, Peng M, Xu A, Lyu J. Associations of air pollution with all-cause dementia, Alzheimer's disease, and vascular dementia: a prospective cohort study based on 437,932 participants from the UK biobank. Front Neurosci. 2023 Aug 4;17:1216686. doi: 10.3389/fnins.2023.1216686. PMID: 37600021; PMCID: PMC10436530.

28. Agrawal S, Schneider JA. Vascular pathology and pathogenesis of cognitive impairment and dementia in older adults. Cereb Circ Cogn Behav. 2022 Jun 30;3:100148. doi: 10.1016/j.cccb.2022.100148. PMID: 36324408; PMCID: PMC9616381.

29. Feng J, Zheng N, Fan X, Li S, Jiang Y, Yi X, Yang H. Association of laxatives use with incident dementia and modifying effect of genetic susceptibility: a population-based cohort study with propensity score matching. BMC Geriatr. 2023 Mar 4;23(1):122. doi: 10.1186/s12877-023-03854-w. PMID: 36870957; PMCID: PMC9985868.

30. Hermann P, Villar-Piqué A, Schmitz M, Schmidt C, Varges D, Goebel S, Bunck T, Lindemann H, Bogner C, Santana I, Baldeiras I, Riggert J, Zerr I, Llorens F. Plasma Lipocalin 2 in Alzheimer's disease: potential utility in the differential diagnosis and relationship with other biomarkers. Alzheimers Res Ther. 2022 Jan 13;14(1):9. doi: 10.1186/s13195-021-00955-9. PMID: 35027079; PMCID: PMC8759265.

31. Paik JS, Ha M, Jung YH, Kim GH, Han KD, Kim HS, Lim DH, Na KS. Low vision and the risk of dementia: a nationwide population-based cohort study. Sci Rep. 2020 Jun 4;10(1):9109. doi: 10.1038/s41598-020-66002-z. PMID: 32499618; PMCID: PMC7272467.

32. Ahmad R, Chowdhury K, Kumar S, Irfan M, Reddy GS, Akter F, Jahan D, Haque M. Diabetes Mellitus: A Path to Amnesia, Personality, and Behavior Change. Biology (Basel). 2022 Feb 28;11(3):382. doi: 10.3390/biology11030382. PMID: 35336756; PMCID: PMC8945557.

33. Chen TS, Mi NN, Lao HY, Wang CY, Lo WLA, Mao YR, Tang Y, Pei Z, Yuan JQ, Huang DF. Investigating the nexus of metabolic syndrome, serum uric acid, and dementia risk: a prospective cohort study. BMC Med. 2024 Mar 13;22(1):115. doi: 10.1186/s12916-024-03302-5. PMID: 38481272; PMCID: PMC10938845.

34. Mühlbauer V, Möhler R, Dichter MN, Zuidema SU, Köpke S, Luijendijk HJ. Antipsychotics for agitation and psychosis in people with Alzheimer's disease and vascular dementia. Cochrane Database Syst Rev. 2021 Dec 17;12(12):CD013304. doi: 10.1002/14651858.CD013304.pub2. PMID: 34918337; PMCID: PMC8678509.