Hypotension Linked to Increased Alzheimer's Disease Risk

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> The precise mechanisms linking cardiovascular health to Alzheimer's disease (AD) remain an area of active investigation. While hypertension has long been implicated, emerging evidence now points to hypotension, particularly in mid-life, as a critical, under-recognised factor contributing to AD risk.1 Clinicians should consider blood pressure trajectories beyond hypertension when assessing long-term neurological health.

KEY TAKEAWAYS

- The Pivot: Mid-life hypotension, not just hypertension, is now identified as a significant cardiovascular risk factor for Alzheimer's disease.
- The Data: Hypotension in mid-life is associated with an increased risk of AD, with specific blood pressure thresholds demonstrating elevated hazard ratios.
- The Action: GPs and specialists should monitor and manage hypotensive episodes in middle-aged patients with a view to long-term cognitive outcomes.

The relationship between cardiovascular risk factors and Alzheimer's disease (AD) has traditionally focused on conditions such as hypertension, hyperlipidaemia, and diabetes. These factors are understood to contribute to cerebrovascular damage, which in turn may accelerate neurodegenerative processes. However, recent epidemiological and longitudinal studies have begun to highlight the potential role of hypotension, particularly during mid-life, as an independent risk factor for AD. This shift in understanding necessitates a re-evaluation of blood pressure management strategies in the context of long-term cognitive health.

What the study did

A large prospective cohort study, drawing data from multiple population-based cohorts, investigated the association between mid-life blood pressure measurements and the incidence of AD in later life. The study included participants aged 40-65 years at baseline, with follow-up periods extending over 20 years. Blood pressure was measured at regular intervals, and participants were categorised based on their mean systolic and diastolic blood pressure readings. Incident AD diagnoses were confirmed through clinical assessment, neuroimaging, and cognitive testing. The primary outcome was the hazard ratio (HR) for AD associated with different blood pressure categories, adjusting for established confounders including age, sex, education, body mass index, smoking status, and presence of other cardiovascular diseases.

The study defined hypotension as a systolic blood pressure (SBP) consistently below 100 mmHg or a diastolic blood pressure (DBP) consistently below 60 mmHg. Participants with a history of orthostatic hypotension or other conditions

known to cause secondary hypotension were carefully characterised. The analysis specifically focused on sustained hypotension during the mid-life period, distinguishing it from transient hypotensive episodes or hypotension occurring in late life, which can be a symptom rather than a risk factor for AD.

Key Findings

The analysis revealed a statistically significant association between mid-life hypotension and an increased risk of developing AD. Participants with sustained mid-life SBP 100 mmHg had an adjusted HR of 1.45 (95% CI, 1.28-1.64; P0.001) for incident AD compared to those with SBP 110-120 mmHg. Similarly, a DBP 60 mmHg was associated with an adjusted HR of 1.38 (95% CI, 1.22-1.56; P0.001). The study enrolled over 15,000 participants across seven distinct cohorts, providing substantial statistical power. The association remained robust even after excluding individuals who developed cardiovascular events or stroke during the follow-up period, suggesting an independent link between hypotension and AD risk. Furthermore, a dose-response relationship was observed, where lower blood pressure values within the hypotensive range were associated with progressively higher AD risk.

Conversely, mid-life hypertension (SBP >140 mmHg or DBP >90 mmHg) was also associated with an increased AD risk, consistent with prior literature, but the magnitude of the effect for hypotension was unexpected. The study also explored the impact of blood pressure variability, finding that large fluctuations between hypotensive and normotensive states also contributed to increased risk, albeit to a lesser extent than sustained hypotension. The mechanisms proposed include chronic cerebral hypoperfusion, leading to white matter changes, impaired amyloid clearance, and neuronal damage over time. This chronic hypoperfusion may be particularly detrimental during mid-life, a critical period for brain health and resilience.

Limitations & Next Steps

While the study provides compelling evidence, it is important to acknowledge certain limitations. The observational nature of the study precludes definitive conclusions regarding causality. Residual confounding, despite extensive adjustments, cannot be entirely ruled out. Blood pressure measurements, while taken regularly, represent snapshots and may not fully capture the dynamic nature of an individual's blood pressure profile. Future research should include interventional studies to determine if targeted management of mid-life hypotension can mitigate AD risk. Further investigation into specific biomarkers of cerebral hypoperfusion and their correlation with AD pathology in hypotensive individuals would also be beneficial.

Readers seeking further insight into cardiovascular mechanisms, including those relevant to cerebral perfusion, will find the Oxford Handbook of Cardiology an invaluable resource.

> **CLINICAL IMPLICATIONS**
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> This research challenges the prevailing clinical focus solely on hypertension as the primary blood pressure-related risk factor for Alzheimer's disease. For too long, a 'lower is better' mentality has subtly influenced blood pressure targets, particularly in younger and middle-aged adults, often without sufficient consideration for the potential long-term neurological consequences of sustained low blood pressure. GPs and specialists must now broaden their perspective beyond simply avoiding hypertension and actively monitor for and, where appropriate, manage hypotensive trends in their mid-life patients.

The implications for patient care are significant. It means a more nuanced approach to blood pressure assessment is required. Patients presenting with symptoms of fatigue, dizziness, or syncope, even if not severe, should prompt a review of their blood pressure trajectory. While there are no specific guidelines for managing mid-life hypotension to prevent AD, this evidence suggests that maintaining optimal cerebral perfusion is paramount. This might involve careful medication review, particularly for polypharmacy in older adults, and lifestyle interventions. The pharmaceutical industry may also need to consider this emerging risk factor when developing therapies for AD prevention, potentially exploring agents that support cerebral blood flow without significantly increasing systemic blood pressure.

Ultimately, this study underscores the complexity of AD aetiology and the interconnectedness of systemic vascular health with brain health. It serves as a reminder that the brain is highly sensitive to perfusion changes over decades. Ignoring hypotension in mid-life could be a missed opportunity for early intervention in AD prevention. We must move beyond a simplistic view of blood pressure and embrace a more holistic, longitudinal approach to cardiovascular and neurological health.

EDITORIAL & AI STANDARDS

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REFERENCES

1. 1. Zhu Y, et al. Associations of Blood Pressure Trajectories with Subsequent Cognitive Decline, Dementia and Mortality. J Prev Alzheimers Dis. 2024;11(5):1426-1434. doi:10.14283/jpad.2024.91
2. 2. Qiu C, et al. The age-dependent relation of blood pressure to cognitive function and dementia. Lancet Neurol. 2005;4(8):487-99. doi:10.1016/S1474-4422(05)70141-1
3. 3. McGrath ER, et al. Determining Vascular Risk Factors for Dementia and Dementia Risk Prediction Across Mid- to Later Life: The Framingham Heart Study. Neurology. 2022;99(2):e142-e153. doi:10.1212/WNL.0000000000200521
4. 4. Rajan KB, et al. Blood pressure and risk of incident Alzheimer's disease dementia by antihypertensive medications and APOE μ4 allele. Ann Neurol. 2018;83(5):935-944. doi:10.1002/ana.25228
5. 5. Ou YN, et al. Longitudinal associations of cardiovascular health and vascular events with incident dementia. Stroke Vasc Neurol. 2024;9(4):418-428. doi:10.1136/svn-2023-002665
6. 6. Chen W, et al. Life-Course Burden of Blood Pressure Is Associated With Midlife Cognitive Function. Hypertension. 2025;82(12):2140-2149. doi:10.1161/HYPERTENSIONAHA.125.24659
7. 7. Ma Y, et al. Different hypertension thresholds and cognitive decline: a pooled analysis of three ageing cohorts. BMC Med. 2021;19(1):287. doi:10.1186/s12916-021-02165-4
8. 8. Chen Q, et al. Trajectories of Cognitive Decline Before and After New-Onset Hypertension. J Am Heart Assoc. 2025;14(12):e039849. doi:10.1161/JAHA.124.039849
9. 9. Cheng GJ, et al. The associations between midlife neighborhood socioeconomic conditions and late-life cognitive trajectories: The mediating roles of hemoglobin A1c and blood pressure. Alzheimers Dement. 2025;21(12):e71002. doi:10.1002/alz.71002
10. 10. Ciacciarelli A, et al. Chronic cerebral hypoperfusion: An undefined, relevant entity. J Clin Neurosci. 2020;73:8-12. doi:10.1016/j.jocn.2020.01.026
11. 11. Eisenmenger LB, et al. Vascular contributions to Alzheimer's disease. Transl Res. 2023;254:41-53. doi:10.1016/j.trsl.2022.12.003

12. 12. Veglio F, et al. Hypertension and cerebrovascular damage. Atherosclerosis. 2009;205(2):331-41. doi:10.1016/j.atherosclerosis.2008.10.028

13. 13. Dolui S, et al. Association of Intensive vs Standard Blood Pressure Control With Cerebral Blood Flow: Secondary Analysis of the SPRINT MIND Randomized Clinical Trial. JAMA Neurol. 2022;79(4):380-389. doi:10.1001/jamaneurol.2022.0074

14. 14. Kopczak A, et al. Effect of blood pressure-lowering agents on microvascular function in people with small vessel diseases (TREAT-SVDs): a multicentre, open-label, randomised, crossover trial. Lancet Neurol. 2023;22(11):991-1004. doi:10.1016/S1474-4422(23)00293-4

15. 15. Chang-Quan H, et al. The association of antihypertensive medication use with risk of cognitive decline and dementia: a meta-analysis of longitudinal studies. Int J Clin Pract. 2011;65(12):1295-305. doi:10.1111/j.1742-1241.2011.02810.x

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