

Bone-brain Axis In Alzheimer’s Disease: Associations Among Bone Mineral Density, Inflammation, Tau Pathology And Gray Matter Atrophy

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Bone loss may exacerbates inflammation and tau pathology, leading to cortical atrophy and symptomatic deterioration. Bone metabolism markers, particularly bone mineral density, may serve as accessible peripheral indicators of disease severity and interventional target to slow Alzheimer’s disease progression.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Emerging evidence suggests bone-brain axis dysfunction in Alzheimer’s disease (AD). But how bone influence AD pathology, cortical atrophy, and clinical outcomes in AD remain unclear.	A total of 265 patients with AD were recruited, including 133 cases with no osteopenia (AD-nOP) and 132 AD with osteopenia (AD-OP). Bone mineral density (BMD) , serum bone metabolism markers, plasma AD biomarkers and inflammatory factors, structural neuroimaging and clinical symptoms were assessed.	(1) Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) scores were correlated with femoral neck BMD (r = 0.195, PFDR = 0.024; r = 0.156, PFDR = 0.049). Activities of daily living (ADL) score was correlated with serum β-C-terminal telopeptide of type I collagen (β-CTX) level (r = 0.216, PFDR = 0.030). (2) Femoral neck BMD was associated with plasma glial fibrillary acidic protein (GFAP) and hyperphosphorylated tau (P-tau)217 levels (β=-136.326, PFDR = 0.022; β = -1.139, PFDR = 0.022). (3) Femoral neck BMD was correlated with bilateral inferior occipital gyrus (IOG) volume (righ: r=0.266, PFDR=0.034; lef: r=0.294, PFDR=0.021). Serum β-CTX level was correlated with right superior temporal gyrus (STG) volume (r=-0.285, PFDR=0.016). (4) In the association between BMD and MMSE score, chain effect through plasma GFAP level followed by P-tau217 level was significant (β = 1.328, 95% CI = 0.199 to 3.275), chain effect through plasma P-tau217 level followed by left IOG volume was significant (β = 1.331, 95% CI = 0.017 to 4.210). In the association between β-CTX and ADL score, chain effect through plasma P-tau217 level followed by right STG volume was significant (β = 1.440, 95% CI = 0.074 to 3.544). (5) Receiver operating characteristic analyses revealed that femoral neck BMD had the predictive value comparable to plasma P-tau217 (area under the curve : 0.729 vs. 0.739).	Bone loss may exacerbates inflammation and tau pathology, leading to cortical atrophy and symptomatic deterioration. Bone metabolism markers, particularly BMD, may serve as accessible peripheral indicators of disease severity and interventional target to slow AD progression.	[1] ZHI N, REN R, QI J, et al. The China Alzheimer Report 2025 [J]. Gen Psychiatr, 2025, 38(4): e102020. [2] JACK C R, JR., ANDREWS J S, BEACH T G, et al. Revised criteria for diagnosis and staging of Alzheimer’s disease: Alzheimer’s Association Workgroup [J]. Alzheimers Dement, 2024, 20(8): 5143-69. [3] ZHANG F, ZHANG W. Research progress in Alzheimer’s disease and bone-brain axis [J]. Ageing Res Rev, 2024, 98: 102341. [4] KWON M J, KIM J H, KIM J H, et al. The Occurrence of Alzheimer’s Disease and Parkinson’s Disease in Individuals With Osteoporosis: A Longitudinal Follow-Up Study Using a National Health Screening Database in Korea [J]. Front Aging Neurosci, 2021, 13: 786337. [5] JIANG Y L, WANG Z X, LIU X X, et al. The Protective Effects of Osteocyte-Derived Extracellular Vesicles Against Alzheimer’s Disease Diminished with Aging [J]. Adv Sci (Weinh), 2022, 9(17): e2105316. [6] COMPSTON J E, MCCLUNG M R, LESLIE W D. Osteoporosis [J]. Lancet, 2019, 393(10169): 364-76. [7] BHATTQA H P, VASIKARAN S, TRIFONIDI I, et al. Update on the role of bone turnover markers in the diagnosis and management of osteoporosis: a consensus paper from The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO), International Osteoporosis Foundation (IOF), and International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) [J]. Osteoporos Int, 2025, 36(4): 579-608. [8] NOWICKI J K, JAKUBOWSKA-PIETKIEWICZ E. Osteocalcin: Beyond Bones [J]. Endocrinol Metab (Seoul), 2024, 39(3): 399-405. [9] CHEN F P, LIN Y C, LIN Y J, et al. Relationship Between Serum 25-Hydroxyvitamin D and Bone Mineral Density, Fracture Risk, and Bone Metabolism in Adults With Osteoporosis/Fractures [J]. Endocr Pract, 2024, 30(7): 616-23. [10] PALMQVIST S, WHITSON H E, ALLEN L A, et al. Alzheimer’s Association Clinical Practice Guideline on the use of blood-based biomarkers in the diagnostic workup of suspected Alzheimer’s disease within specialized care settings [J]. Alzheimers Dement, 2025, 21(7): e70535. [11] KIM K Y, SHIN K Y, CHANG K A. GFAP as a Potential Biomarker for Alzheimer’s Disease: A Systematic Review and Meta-Analysis [J]. Cells, 2023, 12(9). [12] LEE E H, KWON H S, KOH S H, et al. Serum neurofilament light chain level as a predictor of cognitive stage transition [J]. Alzheimers Res Ther, 2022, 14(1): 6. CONTACT Email: 15136926220@163.com ALZHEIMER’S ASSOCIATION AAIC26