Title: Osteoporosis and Alzheimer's disease (AD) in Older Adults

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Key Highlights:

- Osteoporosis and Alzheimer's disease (AD) are highly prevalent in older adults
- Both Osteoporosis and AD are associated with great disability and medical, social, economic burdens
- A possible relationship between osteoporosis and AD in terms of epidemiology and pathogenesis has been investigated in recent years in epidemiological, clinical and research studies

Introduction

Osteoporosis and Alzheimer's disease (AD) are two common problems in older adult populations (Ruggiero et al., 2024) leading to disability and medical, social, and economic burdens in developing countries (Ruggiero et al., 2024). Their prevalence and incidence are growing significantly due to increasing life expectancy (Wanionok et al., 2024). Although AD and osteoporosis may be seen simply as two distinctive highly prevalent diseases among older adults, in recent years many studies have inquired about a possible relationship between AD and osteoporosis in terms of epidemiology and pathogenesis (Zhang et al., 2024).

There is increasing evidence from basic research to clinical studies that supports some degree of comorbidity between the two diseases (Fehsel et al., 2022). Moreover, a global association between osteoporosis and AD has been found in recent epidemiological studies and meta-analyses (Wanionok et al., 2024).

Osteoporosis and Alzheimer's disease (AD)

Osteoporosis is characterised by low bone mineral density (BMD) and structural deterioration of bone tissue (Zhang et al., 2024) which is due to an imbalance in bone remodelling (Margetts et al., 2024); this can lead to fragility fractures, chronic pain and disability (Margetts et al., 2024). Fragility fractures in older adults typically manifest in major skeletal sites, such as the spine and hip (Ruggiero et al., 2024). Vertebral fractures occur generally before hip fractures but often remain undiagnosed (Wanionok et al., 2024). Although both diseases have higher prevalence in women, current studies point to an association between AD and osteoporosis in both sexes (Zhang et al., 2024). Prospective and retrospective studies suggest that dementia may be an independent risk factor for hip fracture in both women and men, and individuals affected by both dementia and osteoporosis have greatst risk (Ruggiero et al., 2024). Studies show that the incidence of hip fractures among AD patients is three times higher compared with patients without AD pathology (Margetts et al. 2024). Gait dysfunction and impaired cognitive function may have a role in increasing fracture risk (Margetts et al., 2024).

Alzheimer's disease (AD) and Osteoporosis

AD is the most common neurodegenerative disease accounting for 60–70% of cases of dementia (WHO 2023). Studies show that individuals that have experienced fragility fractures have higher susceptibility for developing dementia compared with individuals with no previous fractures (Ruggiero et al., 2024). Epidemiological data show an elevated odds ratio for dementia in individuals aged over 60 with a history of hip and other major fractures (Ruggiero et al., 2024). In addition, some authors agree that fragility fractures may worsen neurodegenerative disorders that can lead to dementia (Ruggiero et al., 2024).

Relation between Osteoporosis and Alzheimer's disease (AD)

As reported by some authors there is evidence supporting a bidirectional relationship between cognitive impairment, dementia, and both fragility fractures and low BMD at an early stage (Ruggiero et al., 2024). Recent epidemiological studies have shown that the occurrence of osteoporosis and bone fractures in AD patients is more than double compared to their AD-free counterparts (Margetts et al., 2024). One-third of people with dementia may experience falls or fractures that require hospitalization which can lead to further bone loss, malnutrition, and sarcopenia due to physical inactivity (Ruggiero et al., 2024). Similarly, low BMD can be found in people with cognitive impairment and both osteoporosis and fragility fractures are seen as independent risk factors for dementia (Ruggiero et al., 2024). From a pathophysiological point of view both diseases share common risk factors, such as age, genetics (Zhang et al., 2024), inflammation, oxidative stress, and reduced estrogen levels (Margetts et al., 2024). The possible role of hormones is supported by the fact that the two conditions predominantly affect women, particularly postmenopause (Margetts et al., 2024). Some authors suggest that cellular energy impairment could be the missing causal link, since glucose metabolism is involved in both diseases; a reduction in substrate availability could lead to both bone and brain dysfunction (Fehsel et al., 2022).

Prevention and therapy

Physical activity, fall prevention and fortified nutrition are non-pharmacological measures suggested to prevent or slow down the onset of osteoporosis and dementia (Zhang et al., 2024). Pharmacological options for osteoporosis (particularly postmenopausal) are divided into three different treatment categories: antiresorptive agents, drugs with bone tissue anabolic effects and calcium and vitamin D supplements (Wanionok et al., 2024). However, despite the association between AD and increased fracture risk, osteoporotic patients appear under-treated (Margetts et al., 2024); studies show that only a minority of patients receive calcium and vitamin D, and even less patients receive other osteoporosis medications prior to sustaining a fracture (Margetts et al., 2024).

Conclusion

Osteoporosis and Alzheimer's disease (AD) are highly prevalent among older adults, which can interplay and lead to major disability and social burdens. Although the causal link is still missing, there is increasing evidence from epidemiological and clinical research studies that the association between the osteoporosis and AD might not be casual.

For further reading:

Ruggiero C, Baroni M, Xenos D, Parretti L, Macchione IG, Bubba V, Laudisio A, Pedone C, Ferracci M, Magierski R, Boccardi V, Antonelli-Incalzi R, Mecocci P. Dementia, osteoporosis and fragility fractures: Intricate epidemiological relationships, plausible biological connections, and twisted clinical practices. Ageing Res Rev. 2024 Jan;93:102130. doi: 10.1016/j.arr.2023.102130. Epub 2023 Nov 27. PMID: 38030092.

Wanionok NE, Morel GR, Fernández JM. Osteoporosis and Alzheimer´s disease (or Alzheimer´s disease and Osteoporosis). Ageing Res Rev. 2024 Aug;99:102408. doi: 10.1016/j.arr.2024.102408. Epub 2024 Jul 3. PMID: 38969142.

Zhang F, Zhang W. Research progress in Alzheimer's disease and bone-brain axis. Ageing Res Rev. 2024 Jul;98:102341. doi: 10.1016/j.arr.2024.102341. Epub 2024 May 15. PMID: 38759893.

Fehsel K, Christl J. Comorbidity of osteoporosis and Alzheimer's disease: Is `AKT `-ing on cellular glucose uptake the missing link? Ageing Res Rev. 2022 Apr;76:101592. doi: 10.1016/j.arr.2022.101592. Epub 2022 Feb 19. PMID: 35192961.

Margetts TJ, Wang HS, Karnik SJ, Plotkin LI, Movila A, Oblak AL, Fehrenbacher JC, Kacena MA. From the Mind to the Spine: The Intersecting World of Alzheimer's and Osteoporosis. Curr Osteoporos Rep. 2024 Feb;22(1):152-164. doi: 10.1007/s11914-023-00848-w. Epub 2024 Feb 9. PMID: 38334917; PMCID: PMC10912148.

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Laura Valzolgher is a medical doctor specialized in Dietetics and Clinical Nutrition, and Internal Medicine with special subspecialization in Geriatric Medicine. She also completed her Master of Science in Psychogeriatrics. After working at the Memory Clinic of the Geriatric Department she is currently engaged at the Service of Dietetics and Clinical Nutrition at the Central Hospital of Bolzano in South Tyrol and is temporary Professor in Geriatrics at the University for Nursing Sciences Claudiana (Univr-Bolzano).