Decreased handgrip strength and increased hip osteoporosis in patients with Alzheimer's disease

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ABSTRACT

Objectives: To evaluate the causes of disability in the musculoskeletal system, and depression in patients with Alzheimer's disease (AD) and healthy controls.

Methods: A case-controlled study in which healthy elderly patients (n=56) and patients with AD (n=75) attending the Geriatric Rehabilitation Unit of Ankara Education and Research Hospital, Department of Physical Medicine and Rehabilitation were compared on several measures of disability including handgrip strength, knee x-rays graded for osteoarthritis, dual-energy x-ray absorptiometry results for osteoporosis, and depression scores in the training period of 2003-2004.

Results: Handgrip strength values were significantly lower in patients with AD compared to the controls (19.4 versus 37 pounds force). Osteoporosis in the femoral neck was also more prominent in patients with AD compared to controls (T-scores: -2.1 versus -1.2). Handgrip strength was moderately correlated with femoral neck T-scores (r=0.6, *p*=0.001).

Conclusion: Strategies should be developed to protect patients with AD from osteoporosis and reduced muscle strength.

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Alzheimer's disease (AD) is the most common neurodegenerative disorder characterized by progressive cognitive and physical disability in the elderly.[1] Although there is no cure for AD, co-morbid medical and psychiatric conditions should be identified and optimally treated to minimize excess disability.[2] Therefore, before pharmacologic intervention is instituted, it is important that sources of excess disability and co-morbidity be eliminated or reduced.[2,3] There were several studies that assessed both disability and depression seen in AD.[4-8] However, multi-faceted disability also including the musculoskeletal system has not been reported. Vitamin deficiency and reduced bone mineral density (BMD) were also reported in some studies.[9-11] But multi-system disability evaluations of these geriatric patients were lacking in these studies. For this aim, we studied handgrip strength for the upper extremity, radiographic grade of knee osteoarthritis (OA) for the lower extremity, dual-energy X-ray absorptiometry (DEXA) for osteoporosis, and geriatric depression scale (GDS) for depression in home-living, ambulatory, voluntarily elderly patients with mild to moderate AD and healthy controls in a geriatric rehabilitation unit.

Methods. Totally, 131 elderly patients (75 patients with AD and 56 controls) admitted to the Geriatric Rehabilitation Unit were included in this study after giving informed consent in the training period from September 2003 to July 2004. Ethical approval was received from the Institutional Review Board to carry out this research. All individuals admitted to hospital were ambulatory, living at home and had sought help for some minor difficulties in independent mobility and activities of daily living. They had no past medical history of immobilization and chronic metabolic or inflammatory diseases. Patients with AD were referred from the Department of Neurology for geriatric and cognitive rehabilitation such as psychosocial evaluation, geriatric pain analysis, musculoskeletal examination, osteoporosis, and osteoarthritis management, environmental modifications, posture and balance training. The inclusion criteria for AD were those identified by 1) The Diagnostic and Statistical Manual of Mental Disorders, 4th ed, revised for Dementia,[12] and 2) The National Institute of Neurological and Communicative Disorders and Stroke, Alzheimer's disease and related disorders Association for Alzheimer's disease.[13] All the controls had been referred from the Department of Physical Medicine and Rehabilitation for the management of back pain. Comprehensive laboratory and cranial CT studies were made for all patients with AD and controls. The exclusion criteria for both patients with AD and controls were those identified by 1) medical illnesses, possibly causing cognitive impairment or white matter lesions, including demyelinating diseases, thyroid diseases, 25 (OH) D3 and B12 vitamin deficiencies, and malignant diseases with and without anti-neoplastic agents, 2) focal brain lesions, including lacunar infarcts, and hematoma, 3) complications of developmental abnormalities, mental diseases, substance abuse, or significant neurological antecedents, such as brain trauma, brain tumor, epilepsy and inflammatory diseases, 4) evidence of severe intracranial or cervical arterial occlusive lesions. We assessed the cognitive function of the patients with the mini-mental state examination.[14] The level of depression was evaluated by using the geriatric depression inventory.[15] Bone mineral density measurements were carried out by using Lunar DEXA IQ (Madison, Wisconsin, USA) bone mineral densitometry system for the measurement of bone mineral density. Antero-posterior lumbar spine (L2-L4) and right proximal femur were scanned in each person. Young-adult comparisons (T-score) and same-age comparisons (Z-score) of individual bone mineral density (g/cm^2) were recorded. Weight-bearing double-aspect x-rays of both knees were graded according to the Kellgren-Lawrence osteoarthritis (OA) assessment.[16] Handgrip strength was evaluated by JAMAR hand dynamometer (Jackson, Minnesota, USA) as the mean pounds force of 3 sequential measurements with 30 seconds resting time, with the patient sitting, shoulder adducted, elbow 90˚ degree flexed, and wrist neutrally positioned.

With the SPSS 11.0 package program, comparisons between groups by ANOVA as parametric tests and Wilcoxon as non-parametric tests and correlations between different variables by Pearson' correlation were used for statistical analyzes. Logistic regression analyses for the dependent variables (femur neck t- and z-scores) were applied to detect the independent predictors.

Results. The demographics, the percentage of educational attainment, poly-pharmacy, mini-mental state examination (MMSE) and geriatric depression scores (GDS) are shown in **Table 1**. There were no differences between groups except in MMSE scores. The musculoskeletal system measurements, including DEXA scores, radiographic grading of the knee OA, and handgrip strength are shown in **Table 2**. We detected statistically significant differences between groups in femoral neck T-score, and handgrip strength. The mean and standard deviation of femur neck T-score in AD and control groups were -2.1±0.9 and -1.2±1, (t=-2.15, p=0.032), indicating that patients with AD had lower T-score and lower bone-mineral density compared to controls. Patients with AD had lower handgrip strength in both left, and right hands compared to controls. We detected statistically significant correlations between handgrip strength and femoral neck T-scores (r=0.6, p=0.001) in logistic regression analyses in patients with AD.

Discussion. Buchner and Wagner[17] defined frailty as "the state of reduced physiologic reserve associated with increased susceptibility to disability." When subjects drop below a certain level, they have difficulty getting back to the minimal strength or aerobic capacity required to carry out their ordinary functions or activities of daily living. There is a threshold of relative strength below which subjects are likely to see themselves as impaired, and this threshold is lower in older subjects than in younger

Table 1 - The demographics, level of education, poly-pharmacy, geriatric depression screening, and MMSE scores in patients with AD and controls.

Variable	AD mean ± SD (min-max)		Controls mean ± SD (min-max)		*P*-value
Age (years)	70.6 ± 5.7	(65-87)	69.1 ± 4.3	(65-89)	0.56
Gender (Female %)	88%		89.3%		0.18
BMI (kg/m^2)	29.1 ± 4.1	(18-37)	26.9 ± 4.1	(21-33)	0.17
Primary school %	61.3%		57.1%		0.33
Poly-pharmacy %	36%		32.1%		0.99
GDS scores	15.8 ± 8.2	(6-30)	18.9 ± 11.7	(6-30)	0.62
MMSE scores	20.9 ± 3.3	(11-23)	28.8 ± 3.7	(25-29)	0.01*

MMSE – mini mental state exam, BMI - body mass index, GDS - geriatric depression score, AD - Alzheimer's disease, *significant value geriatric subjects. The geriatric population consists of vigorous or frail elderly people. Frail elderly people have multiple chronic diseases leading to increased morbidity and mortality. It is well known that muscle mass and strength decrease with aging by approximately 1-2% per year in the healthy elderly.[18] We found that handgrip strength was more decreased in patients with AD compared with elderly controls with back pain. Neurodegenerative changes in the primary motor cortex seen in AD may be responsible for this difference. Actually, patients with AD may have decrements in handgrip strength due to problems with performing the measure. Sarcopenia, aging related decrease in muscle mass and quality, characterized by mainly type II fiber atrophy has been linked to osteoporosis.[19-22] Decreased strength and power noted in sarcopenia and additional balance problems contribute to the high incidence of accidental falls and hip fractures observed among the elderly.[23-25] The major limitation of this study was the ignorance of body composition (for example, fat-free and fat mass). We should have evaluated the body composition to determine sarcopenia, as sarcopenia, osteoporosis, cognitive and balance problems may multi-plicate the risk of hip fracture seen in AD. There are a limited number of studies on AD and sarcopenia. Gillette-Guyonnet et al[26] found no statistically significant difference of sarcopenia prevalence in their study including 32 patients with AD and 32 age-, sex- and bone mineral density-matched controls (40.6% versus 21.9%). However, our patients with AD had lower femoral neck T-scores compared to the healthy elderly. The selection of BMD-matched controls in their study may explain these different results. Weller et al[27] reported an independent relation between AD and hip fractures in 1513 elderly Canadians for the National Population Survey for Health Institution. Sato et al[9] reported a similar result in 2nd metacarpal computed x-ray densitometry, with also a correlation between vitamin K and 25 (OH) D3 deficiencies in 100 Japanese women with AD. More accurate detection methods of osteoporosis, such as DEXA or quantitative computed tomography (QCT) were not used in these studies. In addition, 2nd metacarpal densitometry may not predict hip fracture, which leads to significant mortality and morbidity in the elderly.

We found a moderate correlation between handgrip strength and femoral neck T-scores. As a matter of fact, handgrip strength may not reflect muscles of the hip region. It would be better if we could demonstrate the relationship between leg muscle strength and femoral neck BMD T-score. However, we thought that handgrip strength might reflect function in daily living activities. Iwamoto et al[28] reported a similar relationship between handgrip strength and forearm BMD in 979 Japanese postmenopausal women with and without knee OA. We also showed this relation between handgrip strength and hip T-scores in patients with AD.

Similarly, Bean et al[29] investigated handgrip strength in older people without dementia and they found that handgrip was significantly lower in the cases with hip fracture than in the controls without hip fracture.

Interestingly, Milne & Maule[30] reported in their 5-year prospective study that mean handgrip was significantly less at the first examination in those who subsequently

Table 2 - The DEXA results of L2-4 and femoral neck regions, distribution of the radiographic grading of knee osteoarthritis, and handgrip strength measurements of both hands in patients with AD and controls.

DEXA results	Patients with AD (n=75)		Controls (n=56)		*P*-value
L2-4 T-score	-2.3 ± 1.9	(-5.5-2.1)	-1.9 ± 1.3	(-3.5-0.8)	0.65
L2-4 Z-score	-0.5 ± 1.9	(-3.6-3.9)	-0.3 ± 1.3	(-3.1-1.6)	0.62
Femur neck T-score	-2.1 ± 0.9	(-3.8-0.5)	-1.2 ± 1.0	(-3.0-0.9)	0.032*
Femur neck Z-score	-0.5 ± 0.9	(-2.1-1.5)	0.13 ± 0.7	(-1.1-0.9)	0.05
Knee OA gradings %					0.92
Grade I	15 (20%)		14 (25%)		
Grade II	33 (44%)		22 (39.3%)		
Grade III	24 (32%)		14 (25%)		
Grade IV	3 (4%)		6 (10.7%)		
Handgrip strength					
Right handgrip	19.4 ± 5.2	(13-32)	37 ± 14.9	(13-59)	0.002*
Left handgrip	18.2 ± 5.4	(10-31)	38 ± 12.8	(23-59)	0.000*

DEXA – dual-energy x-ray absorptiometry, AD - Alzheimer's disease, OA - osteoarthritis, *significant value died, compared with 5-year survivors. However, handgrip was not significantly related to, or a predictor of dementia in this study. In comparison, Alfaro-Acha et al[31] reported that older Mexican Americans with reduced handgrip strength at baseline demonstrated a statistically significant decline in cognitive function over a 7-year period. They also reported that the hip fracture rate in cognitively impaired subjects was more than 4 times the hip fracture rate for subjects who were not cognitively impaired with the same body mass index (BMI) in non-obese older Mexican Americans.[32]

Strikingly, geriatric depression scores were similar between patients with AD and the healthy elderly controls in our sample. It may depend on similar living place and ages of both groups. Home living with their family may be protective for depression for elderly persons. However, it might be rather speculative because we had neither community dwelling nor nursing home living patients with AD.

The grades of OA in the knee joints were not different between patients with AD and controls. It can be explained by the similar age, gender, and BMI characteristics in both groups. However, no direct comparisons could be carried out with previous reports because the lack of studies on these issues.

Our patients with AD had lower hand grip strength leading to difficulties in activities of daily living. They also had lower hip bone mineral density, a risk for hip fractures. We thought that brisk walking with a partner and supervised upper extremity strength training might be routine exercise programs for patients with AD.

References

1. Kawas LH. Alzheimer's Disease. In: Hazzard WR, Blass JP, Ettinger WH, Halter JB, Ouslander JG, editors. Principles of Geriatric Medicine and Gerontology. New York: McGraw Hill; 1999. p. 1257-1269.
2. Bonner LT, Peskind ER. Pharmacologic treatments of dementia. ***Med Clin N Am*** 2002; 86: 657-674.
3. Taylor DH, Schenkman M, Zhou J, Sloan FA. The relative effect of Alzheimer's disease and related dementias, disability and comorbidities on cost of care for elderly persons. ***J Gerontol B Psychol Sci Soc Sci*** 2001; 56: S285-S293.
4. Regan C, Katona C, Walker Z, Livingston G. Relationship of exercise and other risk factors to depression of Alzheimer's disease: The LASER-AD study. ***Int J Geriatr Psychiatry*** 2005; 20: 261-268.
5. Glaesmer H, Kunstler J, Reuter W. Improvement of functional deficits, physical mobility and cognitive function by treatment in a geriatric day hospital. ***Z Gerontol Geriatr*** 2003; 36: 465-483.
6. Teri L, Gibbons LE, McCurry SM, Logsdon RG, Buchner DM, Barlow WE, et al. Exercise plus behavioral management in patients with Alzheimer's disease: a randomized controlled trial. ***JAMA*** 2003; 290: 2015-2022.
7. Garre-Olmo J, Lopez-Pousa V, Vilalta-Franch J, Turan-Estrada A, Hernandez-Ferrandiz M, Lozano-Gallegom, et al. Evolution of depressive symptoms in Alzheimer's disease: one year follow-up. ***Alzheimer Dis Assoc Disord*** 2003; 17: 77-85.
8. Espiritu DA, Rashid H, Mast BT, Fitzgerald J, Steinberg J, Lichtenberg PA. Depression, cognitive impairment, and function in Alzheimer's disease. ***Int J Geriatr Psychiatry*** 2001; 16: 1098-1103.
9. Sato Y, Honda Y, Hayashida N, Iwamoto J, Kanoko T, Satoh K. Vitamin K deficiency and osteopenia in elderly women with Alzheimer's disease. ***Arch Phys Med Rehab*** 2005; 86: 576-581.
10. Sato Y, Kanoko T, Satoh K, Iwamoto J. Risk factors for hip fracture among elderly patients with Alzheimer's disease. ***J Neurol Sci*** 2004; 223: 107-112.
11. Sato Y, Asoh T, Oizumi K. High prevalence of vitamin D deficiency and reduced bone mass in elderly women with Alzheimer's disease. ***Bone*** 1998; 23: 555-557.
12. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington DC: American Psychiatric Association; 1994.
13. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. ***Neurology*** 1984; 34: 939-944.
14. Folstein MF, Folstein SE, McHugh PR. Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. ***J Psychiatr Res*** 1975; 12: 189-198.
15. Yesavage JA, Brink TL, Rose TL. Development and validation of a geriatric depression screening scale: a preliminary report. ***J Psychiatr Res*** 1982-1983; 17: 37-49.
16. Kellgren JK, Lawrence JS. Radiological assessments of osteoarthritis. ***Ann Rheum Dis*** 1957; 15: 494-501.
17. Buchner DM, Wagner EH. Preventing frail health. ***Clin Geriatr Med*** 1992; 8: 1-17.
18. Skelton DA, Greig CA, Davies JM, Joung A. Strength, power and related functional ability of healthy people aged 65-89 years. ***Age Aging*** 1994; 23: 371-377.
19. Deschenes MR. Effects of aging on muscle fiber type and size. ***Sports Med*** 2004; 34: 809-824.
20. Leveille SG. Musculoskeletal aging. ***Curr Opin Rheumatol*** 2004; 16: 114-118.
21. Carmeli E, Coleman R, Reznick AZ. The biochemistry of aging muscle. ***Exp Gerontol*** 2002; 37: 477-489.
22. Coin A, Sergi G, Beninca P, Lupoli L, Cinti G, Ferrara L, et al. Bone mineral density and body composition in underweight and normal elderly subjects. ***Osteoporos Int*** 2000; 11: 1043-1050.
23. Dutta C. Significance of sarcopenia in the elderly. ***J Nutr*** 1997; 127: 992s-993s.
24. Marcus R. Relationship of age-related decrease in muscle mass and strength to skeletal status. ***J Gerontol A Biol Sci Med Sci*** 1995; 50: 86-87.
25. Clarke MS. The effects of exercise on skeletal muscle in the aged. ***J Musculoskelet Neuronal Interact*** 2004; 4: 175-178.
26. Gillette-Guyonnet S, Nourhashemi F, Andrieu S, de Glisezinski I, Grandjean H, Rolland Y, et al. Determination of appendicular muscle mass by dual-energy x-ray absorptiometry method in women with sarcopenia and Alzheimer disease. ***J Nutr Health Aging*** 2000; 4: 165-169.
27. Weller I, Schatzker J. Hip fractures and Alzheimer's disease in elderly institutionalized Canadians. ***Ann Epidemiol*** 2004; 14: 319-324.

28. Iwamoto J, Takeda T, Ichimura S. Forearm bone mineral density in postmenapausal women with osteoarthritis of the knee. ***J Orthop Sci*** 2002; 7: 19-25.
29. Bean N, Bennett KM, Lehmann AB. Habitus and hip fracture revisited: skeletal size, strength and cognition rather than thinness? ***Age Ageing*** 1995; 24: 481-484.
30. Milne JS, Maule MM. A longitudinal study of handgrip and dementia in older people. ***Age Ageing*** 1984; 13: 42-48.
31. Alfaro-Acha A, Al Snih S, Raji MA, Kuo YF, Markides KS, Ottenbacher KJ. Handgrip strength and cognitive decline in older Mexican Americans. ***J Gerontol A Biol Sci Med Sci*** 2006; 61: 859-865.
32. Alfaro-Acha A, Ostir GV, Markides KS, Ottenbacher KJ. Cognitive status, body mass index, and hip fracture in older Hispanic adults. ***J Am Geriatr Soc*** 2006; 54: 1251-1255.

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