MAYO CLINIC

ORIGINAL ARTICLE

Increased Risk of Osteoporosis in Patients With Depression: A Population-Based Retrospective Cohort Study

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Abstract

Objective: To investigate the relationship between depression and risk of subsequent osteoporosis development.

Participants and Methods: A population-based retrospective cohort analysis was conducted using the Longitudinal Health Insurance Database 2000 of Taiwan. We included 32,978 patients in the depression cohort and 131,912 patients in the no-depression cohort between January 1, 1998, and December 31, 2008, and calculated the incidence rates of newly diagnosed osteoporosis. We used Cox proportional hazards models to assess the effects of depression. The Kaplan-Meier method was applied to estimate the cumulative osteoporosis incidence curves.

Results: Patients with depression were 1.30 times more likely to experience osteoporosis than those without depression. The risk was higher for patients with severe depression and mild depression than for those without depression. A greater hazard ratio magnitude was observed in patients aged 35 to 49 years. We also observed a significant decrease in osteoporosis risk in patients with depression treated with antidepressant agents.

Conclusion: The incidence of osteoporosis in Taiwan is associated with an a priori depression history. The risk was identified in both men and women, particularly in patients aged 35 to 49 years, and was inversely correlated with antidepressant drug treatment.

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Depression, characterized by changes in mood, sleep, self-attitude, cognitive functioning, appetite, and energy level, is a chronic debilitating disease with high prevalence that considerably affects quality of life.[1,2] Osteoporosis is another chronic disease characterized by the systemic impairment of bone mass and microarchitecture, resulting in an increased probability of fragility fractures of the vertebrate, wrist, hip, and other skeletal sites,[3] inevitably augmenting morbidity and mortality in patients.[4]

The relationship between depression and osteoporosis has been demonstrated, but the evidence is heterogeneous.[5-7] Low bone mineral density (BMD), a crucial risk factor for osteoporotic fracture,[8] occurs more frequently in depressed individuals than in the general population.[9-11] The relationship between depression and BMD has been demonstrated in elderly white women[12] and in Asian men.[13] Several authors have suggested that the correlation between BMD and major depressive symptoms is stronger in women compared with that in men.[14] In contrast, an association of a major depressive episode with BMD in young and older male adults has been described in population-based studies.[15-17]

Because depression and osteoporosis are chronic diseases that affect large populations as well as morbidity and quality of life, verifying the association between depression and a posteriori osteoporosis incidence is essential. No epidemiologic study has investigated this relationship in Taiwan. To evaluate the possibility of an association between osteoporosis and depression, we compared the incidence of osteoporosis in patients with and without depression and in patients with depression treated and untreated with antidepressant agents by using data from the National Health Insurance Research Database (NHIRD) of Taiwan.

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PARTICIPANTS AND METHODS

Data Sources

The Taiwanese government launched the National Health Insurance (NHI) program in March 1995, which covered approximately 99% of the 22.96 million people in Taiwan by the end of 2007.[18] The NHIRD contains registration files and original claims data for reimbursement for all beneficiaries enrolled in the NHI program in Taiwan. The Longitudinal Health Insurance Database 2000 (LHID2000), a subset of the NHIRD, contains all original claims data for 1,000,000 beneficiaries enrolled in 2000 randomly sampled from the 2000 Registry for Beneficiaries of the NHIRD, where registration data for every beneficiary of the NHI program between January 1, 1996, and December 31, 2011, were drawn for random sampling. There are approximately 27.38 million individuals in this registry (NHIRD). All the registration and claims data for these 1,000,000 individuals collected by the NHI program constitute the LHID2000. There was no significant difference in the sex distribution (χ^2=0.067; *df*=1; *P*=.80) between patients in the LHID2000 and the NHIRD.[19] We used the January 1, 1996, through December 31, 2011, registry data sets (LHID2000) for beneficiaries, outpatient care based on visits, inpatient care according to admission, and the catastrophic illness database. To protect patient privacy, the data on patient identities were scrambled cryptographically by the NHIRD. The registry for beneficiary data includes scrambled individual identification numbers that can interlink with these data sets. Individual health status was identified from the data according to the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*. The diagnoses of osteoporosis and depression were based on the *ICD-9* codes, which were determined by related specialists and physicians according to the standard imaging and clinical criteria. We obtained approval for this study from the institutional review board of China Medical University Hospital.

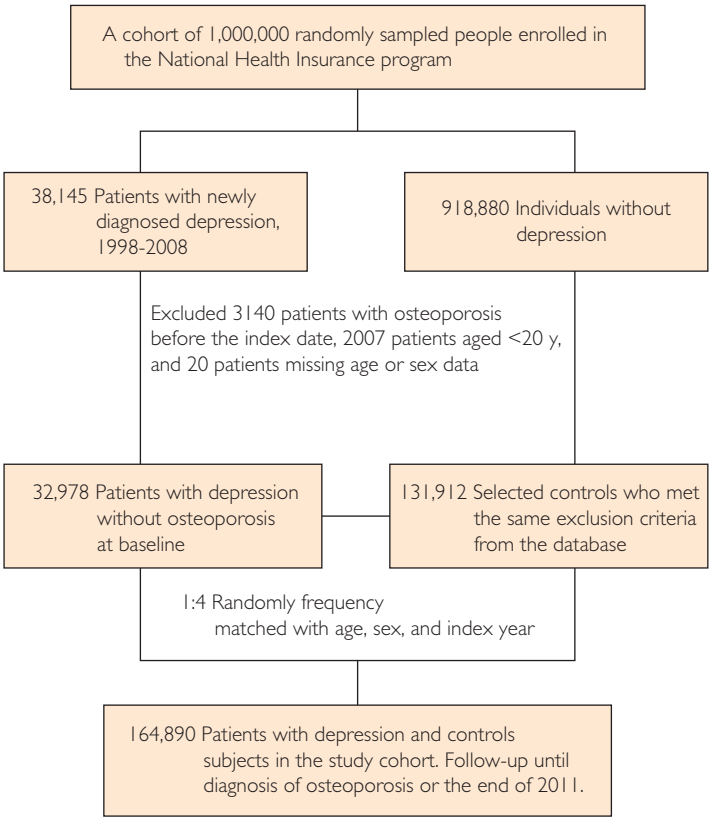

FIGURE 1. The participant selection process in the 2 study cohorts.

Study Participants

Figure 1 shows the selection process of the participants in the 2 study cohorts. We identified 32,978 patients 20 years or older with newly diagnosed depression (*ICD-9-CM* codes 296.2, 296.3, 300.4, and 311) but without a history of osteoporosis between January 1, 1998, and December 31, 2008 (records with missing information on sex or age were excluded), and we defined depression diagnosis data as the index date. Study participants with the diagnosis of depression between January 1, 1996, and December 31, 1997, were excluded at baseline to identify patients with newly diagnosed depression between January 1, 1998, and December 31, 2008. Therefore, the cohort in this study represents the incidence, instead of the prevalence, of depression because most of the prevalence cases of depression were not likely to be included in the study cohort. We divided the patients with depression into 2 subgroups according to severity level. We identified patients with severe depression from the catastrophic illness database and inpatient care data with *ICD-9-CM* codes 296.2 and 296.3 and patients with mild depression from the ambulatory data (*ICD-9-CM* codes 296.2, 296.3, 300.4, and

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