

• Original article •

Prevalence of osteopenia and osteoporosis and factors associated with decreased bone mineral density in elderly inpatients with psychiatric disorders in Huzhou, China

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Background: Little is known about the risks of bone fractures in elderly patients with mental disorders in China.

Aim: Assess the bone mineral density (BMD) of elderly patients with mental disorders in China and identify factors that are associated with low BMD, osteopenia and osteoporosis.

Methods: one hundred and two psychiatric inpatients 60 years of age or older (including patients with schizophrenia, depression, bipolar disorder and dementia) were randomly selected from patients in the geriatric wards of the Third People's Hospital of Huzhou. Detailed demographic, clinical and biometric data were obtained and the BMD of the lumbar spine was assessed using standard dual energy X-ray absorptiometry (DXA) procedures. Based on WHO criteria, individuals with BMD 1 to 2.5 standard deviations below the mean value for healthy young adults were diagnosed as osteopenia and those with BMD values 2.5 or more standard deviations below the mean value were diagnosed as osteoporosis.

Results: The prevalence of osteopenia was 33.3% (95% CI, 24.4%-43.2%) and the prevalence of osteoporosis was 35.3% (26.0%-45.2%) but none of these patients – even the five patients who had had non-traumatic fractures – had ever been treated for these conditions. The prevalence of osteoporosis in females was 10-fold that in males (53% versus 5%). BMD decreased with age and increased with increasing body mass index (a reflection of nutritional status). The prevalence of osteoporosis was much higher in patients with a diagnosis of depression (58%) than in those with schizophrenia (33%), Alzheimer's disease (30%) or bipolar disorder (13%). Regression analyses found that low BMD and the combined category of osteopenia and osteoporosis were both independently associated with female gender, increasing age, decreasing body mass index, and a diagnosis of depression. BMD and osteoporosis were not significantly associated with regular use of antipsychotic medication.

Conclusion: Osteopenia and osteoporosis are common conditions in elderly patients with mental disorders that can seriously affect their quality of life but they often go undiagnosed and untreated. Long-term prospective studies are needed to clarify the relative importance of nutritional status, activity level, medication usage, and other factors in the causal pathways that connect mental illnesses to BMD.

1. Introduction

Bone mineral density (BMD) is a measure of bone mineral content per unit area that reflects the overall strength and brittleness of bone. BMD determination is usually made on cancellous (spongy) bone such as the lumbar spine^[1,2] because the rapid turnover of cancellous bone (versus cortical bone) makes it a more sensitive indicator of metabolic stimuli and other factors

that may affect bone metabolism. The World Health Organization recommends using the dual-energy X-ray absorptiometry (DXA) method^[3] for assessing BMD because it is rapid, safe and accurate. Based on WHO diagnostic standards,^[4] osteopenia (bone mass loss) occurs when BMD is 1 to 2.4 standard deviations below the mean BMD of healthy adults of the same gender and race; osteoporosis occurs when BMD is 2.5 standard

doi:10.3969/j.issn.1002-0829.2012.05.003

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deviations (or more) below the mean BMD of healthy adults of the same gender and race.

Many factors affect BMD, notably age, gender, heredity, and medications. When bone mass is lost osteopenia can manifest as bone pain and deformation of the spinal column. The continued gradual loss of bone mass can progress to osteoporosis, when degeneration of the bony microstructure greatly increases the risk of fractures. Physical limitations, fractures and the associated complications of fractures make osteoporosis a serious public health problem that results in substantial morbidity and mortality.^[5] The estimated prevalence of osteoporosis in elderly mainland Chinese is 7%.^[6]

Several studies from other countries report that mental illnesses such as schizophrenia^[7] and depression^[8] are associated with increased rates of osteoporosis and that several classes of psychiatric medications (antipsychotics, antidepressants, antimanic agents, etc.) cause or are associated with declining BMD.^[9-11] But there is little research about the prevalence and risk factors for osteoporosis in Chinese patients with mental disorders. This basic epidemiological information will be needed before it will be possible to develop targeted interventions.

The current study assesses BMD in psychiatric inpatients 60 years of age or older treated in the geriatric psychiatry wards of the Third People's Hospital in Huzhou, Zhejiang Province.

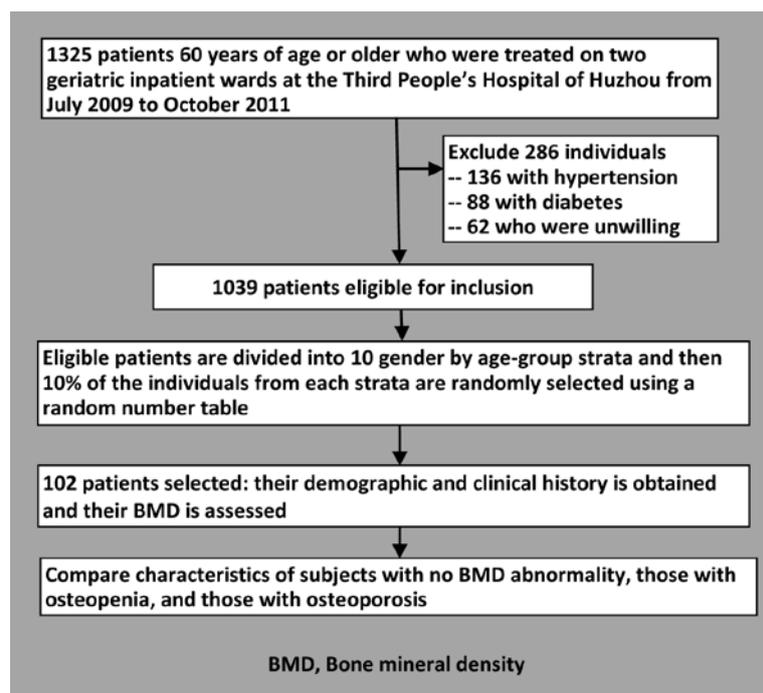
2. Methods

2.1 Subjects

The identification of subjects for the study is shown in Figure 1. Patients treated on the geriatric psychiatric wards of the Third People's Hospital of Huzhou from July 2009 to October 2011 who did not have somatic diseases that could affect bone metabolism and who provided written consent to participate (or whose family guardian provided written consent) were potential participants in the study. A stratified random sample of 102 participants was selected from the eligible pool of 1039 patients.

The characteristics of the participating patients are shown in Table 1. The majority were women. They were 60 to 87 years of age, their body mass index ranged from 14.1 to 38.1 kg/m², and the duration of their current hospitalization at the time of enrollment in the study ranged from 2 to 19 days. The subjects included patients with schizophrenia, depression, bipolar disorder and Alzheimer's disease. The diagnoses were determined by attending-level psychiatrists who employed the diagnostic criteria in the third edition of the Chinese Classification and Diagnostic Criteria of Mental Disorders (CCMD-3).^[12] Many of the patients were regularly taking antipsychotic medications; the remainder were primarily being treated with other types of medications (i.e., antidepressants, antimanic agents, etc.). None of the patients were taking calcium supplements or any other treatment for low bone mass.

Figure 1. Identification of study subjects



There were no statistically significant differences between the 102 participants and the 1039 eligible patients in terms of gender, age, body mass index or diagnostic breakdown.

2.2 Procedures

Basic demographic and clinical information were obtained from the medical charts of the patients. This included gender, sex, age, duration of admission, diagnosis and medication history.

All subjects underwent BMD determination by a trained technician in a separate room at the hospital. We used the LUNAR-Bravo dual-energy X-ray absorptiometer (DXA) (GE Healthcare, Madison, WI, USA), with a measurement coefficient of variation of <1% and a phantom accuracy of 0.6%. Determination of the BMD of the anteroposterior portion of the first to fourth lumbar vertebrae (L1-L4) was performed using conventional DXA procedures.^[13] Quality control for the assessment was carried out in strict accordance with the consensus of the International Society for Clinical Densitometry (ISCD).^[13] The results obtained from the apparatus include the BMD (g/cm²) and the T-value for each of the four lumbar vertebra assessed. The T-value is computed by subtracting the mean BMD of healthy young adults of the same sex and race as the subject from the assessed BMD in the subject and then dividing this difference by the standard deviation of the mean value for healthy young adults. The values for healthy young males and females of Han race used in the computations were based on a national sample from mainland China.^[14]

2.3 Classification of results

BMD results were classified according to criteria specified by the WHO.^[4] Patients with a BMD value within 1 standard deviation of that for healthy young adults (i.e., T-value > -1) were classified as having normal bone mass; those with BMD greater than 1 standard deviation but less than 2.5 standard deviations below the mean value for healthy young adults (i.e., -1 > T > -2.5) were diagnosed as osteopenia (low bone mass); those with BMD values 2.5 or more standard deviations below the mean value for healthy young adults (i.e., T < -2.5) were diagnosed as osteoporosis. Individuals who met criteria for osteoporosis and had had one or more non-traumatic fractures were classified as 'severe osteoporosis.' In this study the classification of subjects was based on the average T-value for the four lumbar vertebra assessed.

Age and body mass index (i.e., weight in kilograms/[height in meters]²) were assessed both as categorical and continuous variables. The Treatment Guidelines for Primary Osteoporosis^[3] recommend using 5-year age bands after the age of 60 but small numbers in some of the age bands forced us to collapse our results into three

10-year age bands (60-69, 70-79, and >80). The WHO recommends five BMI categories for the Asia-Pacific area:^[15] low body mass, <18.5 kg/m²; normal body mass, 18.5-22.9 kg/m²; overweight, 23-24.9 kg/m²; obesity I, 25-29.9 kg/m²; and obesity II, ≥30 kg/m². In our sample only 8 cases were classified as Obesity II, so the Obesity I and Obesity II cases were combined in the analysis. Individuals who had regularly used antipsychotic medications over the prior 3 months were classified as 'currently uses antipsychotic medication'; those who used other psychiatric medications or only sporadically used antipsychotic medication in the prior 3 months were classified as 'does not currently use antipsychotic medication'.

2.4 Statistical analysis

The results were analyzed using SPSS version 13.0 (Chicago, IL, USA). Chi-square tests were used to compare categorical variables by gender and for the three classifications of bone mass density (normal, osteopenia, and osteoporosis). Normally distributed continuous variables were compared using t-tests and F-tests. The T-value measure computed from the BMD was not normally distributed so comparison of T-values by gender used a Kolmogorov-Smirnov rank test. If the continuous variables were significantly different in the three groups classified by bone mass, follow-up multiple comparison tests were conducted using the Tukey test. The relationship of age and body mass index to BMD was assessed using Pearson correlation coefficients. Two types of multivariate analysis were conducted. Unconditional backward stepwise logistic regression was used to identify factors associated with 'abnormal BMD' (i.e., comparing the combined group of subjects with osteopenia or osteoporosis to subjects with normal bone mass). And a backward stepwise linear regression model was used to identify factors associated with the level of BMD (i.e., a continuous dependent variable).

This study was approved by the Ethics Committee of the Third People's Hospital of Huzhou.

3. Results

In our sample of 102 hospitalized patients with mental disorders 60 years of age or older, 70 (68.6%) had decreased bone mass (i.e., osteopenia or osteoporosis). The prevalence of osteopenia was 33.3% (95% CI, 24.4 to 43.2%) and that for osteoporosis was 35.3% (CI, 26.0 to 45.2%). Four subjects (3.9%) who met BMD criteria for osteoporosis had previously experienced non-traumatic fractures so they met WHO criteria for severe osteoporosis. One other subject with osteopenia had also previously experienced a non-traumatic fracture.

Comparison of the characteristics of patients with normal bone mass, osteopenia and osteoporosis is presented in Table 1. The prevalence of osteoporosis

in female patients was 10-fold that in male patients, but male patients had a 50% higher rate of osteopenia than female patients. As expected, the prevalence of osteoporosis increases with age and the BMD was negatively correlated with age ($r=-0.36$). Patients with low body mass were much more likely to have osteoporosis so BMD was positively correlated with body mass index ($r=0.38$). Patients with depression had a much higher prevalence of osteoporosis than individuals with other diagnoses. The mean BMD values for pa-

tients with schizophrenia, depression, bipolar disorder and Alzheimer's Diseases were 0.99 (0.21), 0.83 (0.14), 1.04 (0.21) and 0.98 (0.21) g/cm², respectively ($F=4.61$, $p=0.005$). Multiple comparisons using Tukey tests found that BMD in patients with depression was significantly lower than that in patients with bipolar disorder or schizophrenia. There was no significant difference in the prevalence of osteoporosis between patients who did and did not regularly use antipsychotic medications. The mean BMD for patients regularly taking antipsychotic

Table 1. Comparison of the characteristics of elderly patients with mental disorders with normal bone mass to that of patients with osteopenia (decreased bone mass) and osteoporosis

Characteristic	All subjects	Comparison of characteristics by bone mass category			χ^2	p
		Normal bone mass	Decreased bone mass (Osteopenia)	Osteoporosis		
CATEGORICAL VARIABLES						
	<i>n (%)</i>	<i>n (%)</i>	<i>n (%)</i>	<i>n (%)</i>		
Gender						
Male	38 (37.3)	20 (52.6)	16 (42.1)	2 (5.3)	31.13	<0.001
Female	64 (62.7)	12 (18.8)	18 (28.1)	34 (53.1)		
Age (years)						
60-69	57 (55.9)	26 (45.6)	17 (29.8)	14 (24.6)	15.09 ^a	0.005
70-79	25 (24.5)	4 (16.0)	11 (44.0)	10 (40.0)		
≥80	20 (19.6)	2 (10.0)	6 (30.0)	12 (60.0)		
Body mass index (kg/m²)						
<18.5	20 (19.6)	4 (20.0)	2 (10.0)	14 (70.0)	22.33 ^b	0.001
18.5-22.9	42 (41.2)	10 (23.8)	20 (47.6)	12 (28.6)		
23.0-24.9	18 (17.6)	8 (44.4)	8 (44.4)	2 (11.2)		
≥25.0	22 (21.6)	10 (45.5)	4 (18.2)	8 (36.4)		
Diagnosis						
Schizophrenia	42 (41.2)	16 (38.1)	12 (28.6)	14 (33.3)	13.19	0.040
Depression	24 (23.5)	2 (8.3)	8 (33.4)	14 (58.3)		
Bipolar disorder	16 (15.7)	6 (37.5)	8 (50.0)	2 (12.5)		
Alzheimer's disease	20 (19.6)	8 (40.0)	6 (30.0)	6 (30.0)		
Medications						
Regularly uses antipsychotics	53 (52.0)	19 (35.8)	19 (35.8)	15 (28.3)	2.44	0.295
Doesn't use antipsychotics	49 (48.0)	13 (26.5)	15 (30.6)	21 (42.9)		
CONTINUOUS VARIABLES						
	<i>mean (sd)</i>	<i>mean (sd)</i>	<i>mean (sd)</i>	<i>mean (sd)</i>	<i>F</i>	<i>p</i>
Age	71.3 (8.0)	67.3 (5.5)	71.8 (7.6)	74.5 (8.9)	7.94 ^c	0.001
Body mass index (kg/m ²)	22.3 (4.8)	24.6 (5.5)	21.6 (2.6)	20.8 (5.1)	6.46 ^d	0.002
Days of index admission	11.8 (4.7)	12.3 (4.3)	12.5 (4.8)	10.8 (4.8)	1.47	0.234
^a Chi-square for trend for age is 12.88 ($p<0.001$)						
^b Chi-square for trend for body mass index is 6.42 ($p=0.011$)						
^c Tukey multiple comparison tests finds age is significantly greater in the osteoporosis group than in the osteopenia group and age in the osteopenia group is significantly greater than in the normal group						
^d Tukey multiple comparison tests finds body mass index is significantly greater in the normal group than in the osteoporosis and osteopenia groups						

medication was 1.00 (0.20) g/cm² versus 0.92 (0.22) g/cm² for patients taking other types of medications (t=1.84, p=0.068).

As shown in Table 2, the differences by gender were uniform for all four lumbar sites assessed. Elderly female inpatients with mental disorders had lower absolute bone mass (i.e., BMD values) and lower standardized values of bone mass (i.e., T-values, which adjust for differences by gender in each race) than elderly male inpatients with mental disorders.

Table 3 shows the results for the stepwise logistic regression that used abnormal bone mass (combining osteopenia and osteoporosis) as the dependent vari-

able; age, body mass index and duration of current hospitalization as continuous independent variables and; gender, type of mental illness, and use of antipsychotic medication as categorical independent variables. After the duration of current admission and current use of antipsychotic medications dropped out of the model, we found that female gender, increasing age, decreasing BMI and a diagnosis of depression were significantly associated with osteopenia and osteoporosis. A parallel stepwise linear regression analysis using the mean BMD of the four lumbar vertebrae as the dependent variable and the same independent variables identified the same set of factors that were significantly associated with low BMD.(Table 4)

Table 2. Comparison of lumbar spine bone mass between male and female patients

	Bone mass in g/cm ² (mean, sd)		t-value	p	T-value ^a (median, IQR)		Z-value ^b	p
	males (n=38)	females (n=64)			males (n=38)	females (n=64)		
First lumbar vertebra	0.90 (0.26)	0.83 (0.14)	3.65	0.001	-0.4 (-1.4~1.1)	-2.0 (-2.9~-0.3)	-4.83	<0.001
Secondary lumbar vertebra	0.94 (0.25)	0.87 (0.22)	2.28	0.004	-0.1 (-1.3~0.8)	-2.3 (-3.2~-0.5)	-5.11	<0.001
Third lumbar vertebra	0.97 (0.22)	0.89 (0.19)	2.94	0.005	0.1 (-1.3~1.0)	-2.3 (-3.4~-0.7)	-5.57	<0.001
Fourth lumbar vertebra	0.99 (0.21)	0.93 (0.14)	3.86	<0.001	-0.1 (-1.0~1.3)	-2.2 (-2.9~-0.7)	-4.93	<0.001
L1 - L4 ^c	0.97 (0.23)	0.88 (0.18)	4.23	<0.001	0.0 (-1.4~1.0)	-2.3 (-3.1~-0.8)	-5.24	<0.001

IQR, interquartile range
^a The T-value is computed by assessing the difference between the bone mineral density of the subject and the mean value for young healthy adults of the same gender and race and then dividing this difference by the standard deviation of the mean value in the healthy young adult group
^b Based on results of the Kolmogorov-Smirnov rank test
^c The data of 'L1 - L4' is the mean of the four measurements from the first lumbar vertebra to the fourth lumbar vertebra

Table 3. Stepwise logistic regression analysis of factors associated with osteopenia and osteoporosis in elderly individuals with mental illnesses^a

Variables	Regression coefficient (β)	Standard error	Wald value	p-value	OR	95% CI
Female gender	1.77	0.58	9.18	0.002	5.85	1.87-18.35
Age (years)	0.16	0.05	9.56	0.002	1.17	1.06-1.30
Body Mass Index (kg/m ²)	-0.24	0.08	9.78	0.002	0.78	0.67-0.91
Type of mental illness						
Schizophrenia	---	---	---	---	1.00	---
Depression	2.64	1.01	6.88	0.009	14.07	1.95-101.43
Bipolar	-0.16	0.78	0.04	0.835	0.85	0.19-3.89
Dementia	-1.01	0.78	1.70	0.192	0.36	0.08-1.66

OR, odds ratio; 95% CI, 95% confidence interval
^a The R² of this logistic model is 36.6%.

Table 4. Linear regression analysis of factors associated with low bone mass density (BMD) in elderly individuals with mental illnesses^a

Variables	Regression coefficient (β)	Standard error	Wald value	t-value	p-value	95% CI
Female gender	0.164	0.034	0.383	4.87	<0.001	0.097~0.231
Age (years)	0.006	0.002	0.236	3.01	0.003	0.002~0.010
Body Mass Index (kg/m ²)	-0.013	0.003	-0.296	-3.82	<0.001	-0.020~-0.006
Type of mental illness ^b						
Depression	0.095	0.041	0.194	2.29	0.024	0.012~0.117
Bipolar	-0.029	0.047	-0.050	-0.61	0.541	-0.121~0.064
Dementia	-0.015	0.044	-0.029	-0.34	0.734	-0.103~0.073

95% CI, 95% confidence interval

^a Adjusted R² of this equation is 42.8%^b Uses schizophrenia as the comparator

4. Discussion

4.1 Main findings

The overall prevalence of decreased bone mass in these elderly psychiatric inpatients (69%) was higher than the prevalence reported in some community-based studies of elderly persons in China^[16] but lower than the prevalence reported in other community-based studies of elderly persons in China.^[17,18] The reasons for these differences may be related to differences in the age and gender distribution of the samples and in the methodology for assessing BMD.

The linear regression analysis and logistic regression analysis found that low BMD and the combined category of osteopenia and osteoporosis were both independently associated with female gender, increasing age, decreasing body mass index, and a diagnosis of depression. The much higher prevalence of osteoporosis in female patients than in male patients and the relationship of BMD to age and body mass index are robust findings that have been previously reported in China^[16,19] and elsewhere.^[20,21]

The much higher prevalence of osteoporosis and the much lower BMD in patients with depression versus those with the other major diagnoses has been reported in other countries^[8,22-24] but has not, to our knowledge, been previously reported in China. The elderly depressed subjects in this study required psychiatric hospitalization so it is possible that the depressive illness was severe enough to result in poor nutritional status and decreased activity levels. Similarly, some authors^[25,26] consider unhealthy lifestyles a cause of low BMD in patients with schizophrenia. Careful prospective studies will be needed to delineate the hypothesized causal pathways that connect mental disorders such as depression and schizophrenia to low BMD and osteoporosis.

We did not find that regular use of antipsychotic medications was associated with lower BMD or higher rates of osteopenia or osteoporosis. However, our analysis could not provide a definitive answer to the question of the relationship of antipsychotic medication use and BMD because we were comparing those who regularly took antipsychotic medications in the prior 3 months to patients who took other types of psychiatric drugs in the prior 3 months (which may also affect BMD) and because no adjustment was made for the dosage and duration of use of these medications. Several authors suggest that antipsychotic medications can adversely affect bone metabolism via their effects on gonadal function^[21,27] but treatment of psychotic symptoms in elderly patients could also result in improved appetite and, thus, better nutritional status.

4.2 Limitations

Several factors not considered in this preliminary study of osteoporosis in elderly psychiatric patients in China will need to be addressed in subsequent research. The sample was relatively small so the confidence intervals around the estimated prevalence of osteopenia and osteoporosis were quite wide and it was not possible to provide precise rates in different subgroups of patients (by diagnosis, type of medication, etc.). Many factors that could potentially affect BMD were not included in the analysis: duration of illness, activity level, diet, dose and duration of medication usage, tobacco and alcohol use, family history of osteoporosis, and so forth. There was no normal control group to compare these results with elderly Chinese who do not have mental illnesses. This was a cross-sectional study so it was not possible to make any causal inferences about the associations identified. Long-term follow-up studies will be needed to compare the rate of change of BMD in patients with different psychiatric diagnoses and in those exposed to different types of psychiatric medications.

4.3 Significance

The prevalence of low bone mass and osteoporosis identified in these elderly psychiatric patients was quite high but none of them had received treatment for osteopenia or osteoporosis, even though some of them had previously experienced non-traumatic fractures. Osteoporosis is a serious medical condition that significantly decreases the quality of life of elderly individuals so psychiatric clinicians, particularly those that frequently treat geriatric patients, need to periodically assess their patients' BMD and actively treat osteopenia and osteoporosis when they occur.

It remains unclear whether elderly individuals with any mental illness or only those with some specific mental illnesses have higher than expected rates of osteoporosis. There is also continuing controversy about the hypothesized role of antipsychotic medication in the etiology of osteoporosis in patients with mental illnesses. Prospective studies that monitor changes in BMD over the course of illness and during different treatments while controlling for a variety of potential confounding variables (e.g., gender, age, family history, etc.) will be needed to clarify these issues.

Financial support

Support for the study was provided by the Third People's Hospital of Huzhou.

Conflict of interest

The authors report no conflict of interest related to this study.

Funding

This study was supported by a grant from the John Davis foundation (NO. 200603).

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(received: 2012-04-05; accepted: 2012-08-22)



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• 论著 •

湖州市住院老年精神障碍患者骨量减少和骨质疏松的发生率及骨密度下降的相关因素

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摘要

背景 国内对住院的老年精神障碍患者骨折风险的研究较少。

目的 评估老年精神障碍患者的骨密度(bone mineral density, BMD), 探明骨密度降低、骨量减少(osteopenia)和骨质疏松(osteoporosis)的相关因素。

方法 随机选取湖州市第三人民医院老年科精神障碍住院患者(60岁或以上, 诊断为精神分裂症、抑郁症、双相障碍或痴呆)102例。采集患者详细的人口学资料、临床资料、身高和体重指数等, 采用双能X射线吸收测定法(dual energy X-ray absorptiometry, DXA)测定腰椎的骨密度。根据世界卫生组织的标准, 将低于健康成人平均骨密度1~2.5个标准差者判定为骨量减少, 将低于2.5个标准差以上者判定为骨质疏松。

结果 骨量减少的发生率为33.3%(95%CI, 24.4%~43.2%), 骨质疏松的发生率为35.3%(26.0%~45.2%), 所有这些患者均没有因骨密度降低而接受相应治疗, 即便是5例曾发生过非外伤性骨折的患者也不例外。女性骨质疏松的发生率是男性的10倍(53%比5%)。骨密度随年龄的增加而下降, 但随体重指数的增加而增加(患者营养状况改变的结果)。抑郁症患者骨质疏松的发生率(58%)远远高于精神分裂症(33%)、阿尔茨海默病(30%)以及双相障碍(13%)的患者。将骨量减少、骨质疏松患者合并为一组后回归分析发现, 低骨密度和合并组均与女性、年龄大、体重指数低及抑郁症诊断独立相关。骨密度下降及骨质疏松与规律服用抗精神病药不相关。

结论 骨量减少和骨质疏松是老年精神障碍患者常见的问题, 会严重影响其生活质量, 但这些问题往往没有得到诊治。需要进一步开展长期的前瞻性研究, 以便阐明营养状况、活动量、药物使用及其他因素在精神疾病与骨密度下降之间的病因学通路中所起的重要作用。