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A Study of Bone Mineral Density and its Determinants in Type 1 Diabetes Mellitus*

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ABSTRACT Objective: To explore the changes of the bone mineral density (BMD) and the relationship between BMD and clinical related factors in type 1 diabetic patients. **Methods:** BMD in lumbar spine and hip in 108 type 1 diabetic patients and 106 control subjects were measured by using Dual-energy X-ray Absorptiometry (DXA). In all subjects, age, height, body weight, waistline, hips were measured, in type 1 diabetic patients, Diabetes duration and HbA1c were assessed. **Results:** BMDs of lumbar 1 (L1), lumbar 2 (L2), lumbar 3(L3), lumbar 4 (L4), lumbar 1-4 (L1-4) total, Neck, Troch, ward's, Trunk and hip total were significantly lower in type 1 diabetic patients than control subjects. In type 1 diabetic patients, there were significant positive correlation between body mass index (BMI) and BMDs of L1, L2, L1-4 total, Neck, Troch, Trunk and hip total. In type 1 diabetic patients, HbA1c level and age was negatively correlated and BMI was positively correlated with L1-4 total BMD and left hip total BMD ($P<0.05$). Gender was correlated with left hip total BMD ($P<0.05$). **Conclusions:** BMD of type 1 diabetic patients were significantly lower than that of control subjects. Gender, age, BMI and HbA1c were related to the BMD in type 1 diabetic patients.

Key words: Type 1 diabetes mellitus; Bone mineral density; Influencing factor

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Introduction

Type 1 diabetes is an autoimmune disease with absolute lack of insulin that culminates in the destruction of pancreatic β-cells and the development of hyperglycemia, which can affect bone metabolism through different aspects. Large-scale epidemiological survey showed that the incidence of the disease is about 2% to 3% annual rate of growth, the distribution of large differences between the characteristics of each region, in recent years the emerging of type 1 diabetes squint toward young person. Diabetic patients with osteoporosis with decreased bone mineral due to absolute or relative lack of insulin causing content of trace elements in the body's metabolism of sugar, protein, fat metabolism, calcium, phosphorus, magnesium as a result of, or even metabolic pathological fracture bone disease. Impact on bone mineral density in type 1 diabetes research hotspot in recent years, currently abroad on type 1 diabetes research has been carried out multi-ethnic multi-region, found bone mineral density in patients with type 1 diabetes and clinically relevant factors such as body mass index (BMI) findings glycated hemoglobin, duration and other relations are not consistent [1-5], while domestic research on bone mineral density in patients with type 1 diabetes rarely, the lack of a larger study sample, only peng Duan [6], in Nanchang, Jiang xi Province regional bone mineral density in type 1 diabetes and related factors were reported. This paper aims to investigate the effect of changes in bone mineral density in Qingdao, Shandong Province, and clinical factors in patients with type 1 diabetes on bone mineral density in type 1 diabetic patients for early prevention.

1 Materials and Methods

1.1 Subjects

We selected 108 patients with type 1 diabetes in our hospital for treatment of Endocrinology from August 2008 to June 2009, including 64 male cases, 44 female cases, aged (39.81 ± 17.30). Type 1 diabetes diagnosis in 1999 WHO diagnostic criteria. The control group of healthy people contains 106 cases, including 63 males and 43 females, aged (40.10± 18.24). All subjects were excluded affect bone metabolism diseases such as chronic kidney disease, thyroid and parathyroid disorders, pituitary and adrenal disorders, rheumatic diseases, cancer, bone metabolism without taking drugs (such as corticosteroids, estrogen, thyroid hormone, calcitonin, bisphosphonates, antiepileptic drugs, diuretics) and other (such as movement disorders and non-traumatic fracture) cases, with no ketoacidosis and infection within the past 3 months. There were no significant differences ($P>0.05$) in sex and age, and they are comparable.

1.2 Research and Methods

1.2.1 Index detection Index detection, including waist cir-

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cumference, hip circumference, height, weight, and body mass index [BMI = weight (Kg) / height(m^2)].

1.2.2 Bone densitometry Bone mineral density was measured by dual-energy X-ray absorptiometry absorption (DEXA), application U.S. NORLAND XR-36 bone density measuring instrument, measuring lateral lumber spine (L1, L2, L3, L4,L1-4 overall) and the left hip (femoral neck, trochanter, ward's triangle, femoral, and overall left hip) bone density.

1.2.3 Biochemical indicators All subjects morning fasting venous blood, with Backman automatic biochemical analyzer fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), blood urea nitrogen (BUN), creatinine (Cr), uric acid (UA); using high performance liquid chromatography assay of glycated hemoglobin(HbA1c).

1.3 Statistical analysis

Statistical analysis was done by SPSS version 17.0.The mean± standard deviation ($\bar{x}$± SD) was given as descriptive statistics. Two independent samples t-test was used to test the difference among groups; A linear regression analysis was done to assess the individual effect of demographic and laboratory variables on decreased BMD. A P value less than 0.05 was considered significant.

2 Results

2.1 Type 1 diabetes BMD comparison with the control

The BMD of diabetic patients and the control group are presented in Table 1, and the BMD are comparable between patients with diabetes and control subjects. Type 1 diabetic patients had a lower BMD than control subjects at both sites: the spine and The left hip. There was a general trend towards a decrease in BMD in T1D, one hypothesis could be that the complications linked to diabetes (retinopathy, neuropathy, nephropathy, macroand microangiopathy) were responsible for the Decreased BMD. A few studies (Clausen et al.[7], Goliat[8]) addressed nephropathy generally reporting lower BMD in patients with albuminuria than without. One study by Rix et al[9] reported lower BMD in patients with neuropathy than without.

Table 1 Comparison of the diabetes BMD

Groups	Number	L1BMD	L2BMD	L3BMD	L4 BMD	L1-4 total BMD
DM1	108	0.958± 0.153	1.034± 0.163	1.045± 0.167	1.018± 0.172	1.014± 0.162
Control group	106	1.112± 0.163	1.174± 0.170	1.206± 0.181	1.184± 0.189	1.176± 0.168
t		-7.048	-6.108	-6.740	-6.672	-7.105
P		<0.01	<0.01	<0.01	<0.01	<0.01
Groups	Number	Femoral neck BMD	Ward's triangle BMD	Greater trochanter BMD	Femoral BMD	Overall left hip BMD
DM1	108	0.906± 0.158	0.772± 0.207	0.760± 0.146	1.108± 0.191	0.938± 0.154
Control group	106	0.922± 0.145	0.853± 0.187	0.855± 0.136	1.258± 0.198	1.052± 0.153
t		-4.418	-3.022	-4.937	-5.606	-5.393
P		<0.01	0.003	<0.01	<0.01	<0.01

2.2 Multiple regression analysis of each set of clinical indicators Ⅰ diabetes effects on bone mineral density

I diabetes group were to L1-4 overall and left hip BMD overall BMD as independent variables, age, gender, disease duration, height, weight, BMI, HbA1c as the dependent variable regression analysis. L1-4 overall BMD and overall left hip BMD was negatively correlated with HbA1c and age, they were positively correlated with BMI (P<0.05), both independent of the duration; left hip BMD overall was gender-related (P<0.05). Table 2, Table 3.

Table 2 L1-4 BMD affect the overall results of multiple regression factors

Argument	B	SE	Beta	T	P
Duration (months)	0.000	0.000	0.043	0.436	0.664
Sex	-0.013	0.031	-0.04	-0.426	0.671
Age	-0.004	0.001	-0.41	-3.786	0.000
Body weight	-0.027	0.008	-0.116	-3.507	0.001
Height	0.025	0.005	0.791	4.938	0.000
BMI	0.083	0.021	0.673	3.914	0.000
HbA1c	-0.015	0.006	-0.206	2.562	0.012

Table 3 Factors Affecting the left hip BMD overall results of multiple

Argument	B	SE	Beta	T	P
Duration (months)	0	0	-0.113	-1.246	0.216
Sex	-0.065	0.027	-0.208	-2.364	0.020
Age	-0.003	0.001	-0.337	-3.356	0.001
Body weight	-0.010	0.007	-0.844	-1.510	0.134
Height	0.012	0.004	0.878	2.612	0.010
BMI	0.045	0.019	0.054	2.407	0.018
HbA1c	-0.010	0.005	-0.148	-1.985	0.047

3 Discussion

BMD of type 1 diabetic patients were significantly lower than control subjects, which is consistent with the foreign reports[1-4]. ① Type 1 diabetes is caused by destruction of pancreatic β cells leads to an absolute lack of insulin secretion. Insufficient insulin lead to metabolic disorders of the three nutrients stored in the body as the decomposition of protein and amino acids, bone matrix consumption also increased, making the bone matrix due to insufficient bone mineral deposition and lost; insulin deficiency can affect vitamin D metabolism, kidney -α hydroxylation activity, reducing the 1,25- (OH) D3 synthesis to impact the intestinal absorption of calcium which leads to reduced bone mass; osteoblast surface (OB) exists insulin receptor, insulin directly stimulate the synthesis of collagen nucleotide of osteoblasts, increasing deposition of calcium in bones [10], the lack of insulin lead to the reduction of the number of osteoblasts and activity decreased which cause less bone matrix formation and ossification disorders; the absence of insulin inhibit the osteocalcin synthesis of OB that decrease bone update rate and bone formation; The insulin could synergistically promote bone formation synergistic effects with other factors, such as IGF-1[11] and parathyroid hormone(PTH), insulin can be significantly down many organizations, including bone tissue IGF binding protein 1, making the bone cells more sensitive to IGF of the surrounding environment, the lack of such synergies insulin decreased, thus affecting osteoblasts and osteoblast precursor cells proliferation, differentiation and matrix synthesis. ② Youth with type 1 diabetes childhood onset, since the absolute lack of insulin, reducing the rate of bone formation and peak bone mass accumulation in its growth and development [12]. ③ immune factors: Recently skeletal immunology concepts are proposed [13]. Insulin has an important role in maintaining normal lymphocyte activation and immune response and enhancing immune function [14], insulin deficiency can lead to abnormal regulation of the immune system, resulting in excessive inflammatory response factor [interleukin (IL) -1, tumor necrosis factor (TNF)-a, etc.] and promoting the differentiation of osteoclasts, enhancing bone resorption, and inducting bone progressively lost.

The results of this study showed that patients with diabetes type 1 L1-4 BMD and the overall left hip BMD was positively correlated with BMI, which is consistent with the Eller-Vainicher C[2] and Abd El Dayem SM [15]study results. Diabetes type Ⅰ elevated BMI may play a role in protecting bones and reducing fracture risk. Vestergaard et al [1] study showed there is no correlation between BMI and BMD, which may be due to the selected type Ⅰ diabetes mostly normal weight or weight loss, and minor differences in BMI.

The results of this study showed that patients with type 1 diabetes overall L1-4 BMD and left hip BMD were negatively correlated with age and HbA1c. With age increasing, bone mineral density decreased, the study results are consistent with Vestergaard, Strotmeyer etc[16]study, after reaching a peak bone density, increasing with age, constantly losing calcium, bone mass decreased. Negatively correlated with HbA1c levels illustrate that glycemic control play a important role on bone mineral density. Other studies [3,4] showed that the same trend that poor glycemic control is associated with low BMD. Studies in animal models of type 1 diabetes confirmed that glycemic control and BMD are closely related, and conditions associated with fracture healing[17,18]. High blood sugar causes osmotic diuresis, increasing excretion of calcium and phosphorus and high urine sugar block tubular reabsorption of calcium and phosphorus, increasing bone mineral loss, leading to low blood calcium, which increased secretion of parathyroid hormone to stimulate and promote bone resorption, further making BMD decreased [19]; Long-term high blood sugar in diabetic patients can generate a lot of advanced glycation end products, which can enhance osteoclast -induced bone resorption[20]. Therefore, good control of blood glucose reduces bone loss, increases bone strength. The study also showed that the left hip BMD overall gender-related, suggesting the existence of gender differences in hip BMD. Hofbauer[21]and other research shows that men with type 1 diabetes duration was negatively correlated with BMD, and BMD in women with type 1 diabetes had no correlation with the course.

The results of this study shows that the overall L1-4 BMD and overall left hip BMD were independent with duration, and Joshi A, etc. [3] found the same results, but Vestergaard, Strotmeyer [16]showed that age and duration of the display and bone mineral density was positively related. This inconsistency may be related to insufficient sample size. Factors affecting bone mineral density

in type 1 diabetes patients and the exact mechanism needs further study.

References

[1] Ves tergard P. Discrepancies in bone mineral density and fracture risk in patients with type 1 and type 2 diabetes a meta analysis [J]. Osteoporos Int, 2007,18(2): 427-444

[2] Eller-Vainicher C, Zhukouskaya VV, Tolkachev YV, et al. Low bone mineral density and its predictors in type 1 diabetic patients evaluated by the classic statistics and artificial neural network analysis [J]. Diabetes Care, 2011, 34(10): 2186-2891

[3] Joshi A, Varthakavi P, Chadha M, et al. A study of bone mineral density and its determinants in type 1 diabetes mellitus[J]. J Osteoporos, 2013, 2013: 397814

[4] Danielson KK, Elliott ME, LeCaire T, et al. Poor Glycemic Control is Associated with Low BMD Detected in Premenopausal Women with Type 1 Diabetes[J]. J Osteoporos, 2009, 20(6): 923-933

[5] Schwartz AV, Sellmeyer DE. Diabetes, fracture, and bone fragility[J]. Curr Osteoporos Rep, 2007, 5(3): 105-111

[6] Duan Peng, Xu Ping, Wu He-ping, et al. Bone Mineral Density in Patients with Type 1 Diabetes Mellitus and Its Associated Factors[J]. Chiese generral practice, 2013, 16(13): 1007-1010

[7] Clausen P, Feldt-Rasmussen B, Jacobsen P, et al. Microalbuminuria as an early indicator of osteopenia in male insulindependent diabetic patients[J]. Diabet Med, 1997, 14: 1038-1043

[8] Goliat E, Marusza W, Ostrowski K, et al. Microalbuminuria as a risk factor for diabetic osteopathy in patients with IDDM and renal sufficiency[J]. Pol Arch Med Wewn, 1998, 100: 111-118

[9] Rix M, Andreassen H, Eskildsen P. Impact of peripheral neuropathy on bone density in patients with type 1 diabetes[J]. Diabetes Care, 1999, 22: 827-831

[10] Pan H, Wu N, Yang T. Association between bone mineral density and type 1 diabetes mellitus: a meta-analysis of cross-sectional studies[J]. Diabetes Metab Res Rev, 2013, 16 [Epub ahead of print]

[11] Pater A, Odrowąż-Sypniewska G. Alterations of bone metabolism in children and adolescents with diabetes mellitus type 1 [J]. Pediatr Endocrinol Diabetes Metab, 2011, 17(3): 158-161

[12] Ortlepp JR, Metrikat J, Albrecht M, et al. The vitamin D receptor genevariant and physical activity predicts fasting glucose levels in healthy young men[J]. Diabet Med, 2003, 20(6): 451-454

[13] Sato K, Takayanagi H. Osteoclasts, rheumatoid arthritis and immunology[J]. Curr Opin Rheumatol, 2006, 113: 419-426

[14] Stentz FB, Kitabchi AE. Activated T lymphocytes in Type 2 diabetes: implications from in vitro studies[J]. Curent Drug Targets, 2003, 4(6): 493-503

[15] Abd El Dayem SM, El-Shehaby AM, Abd El Gafar A. Bone density, body composition, and markers of bone remodeling in type 1 diabetic patients[J]. Scand J Clin Lab Invest, 2011, 71(5): 387-393

[16] E. Strotmeyer, J. Cauler. Diabetes mellitus, bone mineral density, and fracture risk [J]. Current Opinion in Endocrinology, Diabetes and Obesity, 2007, 14(6): 429-435

[17] Follak N, Kloting L, Wlof E, et al. Delayed remodeling in the early period of fracture healing in spontaneously diabetic BB/OK rats depending on the diabetic state[J]. Histol Histopathol, 2004, 19(2): 473-486

[18] Follak N, Kloting I, Merk H. Influence of diabetic metabolic state on fracture healing in spontaneously diabetic rats[J]. Diabetes Metab Res Rev, 2005, 21(3): 288-296

[19] Gregorio F. Cristallini S. Santeusmtai F, et a1. 0steopenia associated with non-insulin-dependent diabetes mellitus: what are the causes?[J]. Diabetes Res Clin Pract, 1994, 23(1): 43-54

[20] Hein G, Weiss C, Lehmann G, et al. Advanced glycation end product modification of bone proteins and bone remodeling: hypothesis and preliminary findings[J]. Ann Rheum Dis, 2006, 65(1): 101-104

[21] Hofbauer LC, Brueck CC, Singh SK, et al. Osteoporosis in patients with diabetes[J]. J Bone miner Res, 2007, 22: 1317-1328

1 型糖尿病患者骨密度的变化及相关因素分析 *

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摘要 目的:观察 1 型糖尿病患者骨密度(bone mineral density,BMD)的变化及其影响因素。**方法:**采用双能 X 线骨密度仪测定 108 例 1 型糖尿病患者及 106 例非糖尿病人群腰椎 1 至 4(L1、L2、L3、L4、、L1-4 总体)及左侧髋部(股骨颈、大转子、ward's 三角、股骨干及左髋总体)骨密度,同时测定受试者年龄、身高 、体重、腰围、臀围,1 型糖尿病患者病程、糖化血红蛋白(HbA1c)等指标,利用多元回归分析 1 型糖尿病患者骨密度的相关因素。**结果:** L1-4 总体 BMD 和左髋总体 BMD 与年龄、HbA1c 呈负相关,与 BMI 呈正相关(P<0.05);左髋总体 BMD 与性别有关(P<0.05)。**结论:**1 型糖尿病患者 BMD 低于对照人群,1 型糖尿病患者的性别、年龄、BMI、HbA1c 水平与 BMD 关系密切。

关键词:1 型糖尿病;骨密度;影响因素

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