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To Explore the Relationship between Lower Extremity Vascular Sclerosis and Osteoporosis in Elderly Men with Type 2 Diabetes Mellitus

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Abstract

Objective: To investigate the correlation between lower extremity vascular sclerosis and osteoporosis in elderly men with type 2 diabetes mellitus. **Methods:** A total of 359 elderly male patients with type II diabetes hospitalized in the First Affiliated Hospital of Chongqing Medical University from January 2018 to June 2023 were retrospectively collected. According to the BMD (Bone Density Value), the patients were categorized into osteoporotic ($T \leq -2.5$, $n = 248$) and non-osteoporotic groups ($T > -2.5$, $n = 111$). T test and Chi-square test were used to evaluate the differences in clinical data, biochemical markers and ABI between two groups. Multivariate logistic regression was used to analyze the risk factors of osteoporosis in elderly men with type 2 diabetes mellitus. **Results:** Compared with the non-osteoporotic group, the differences in diabetes course, systolic blood pressure, ABI, BMI, uric acid, triglyceride, and HDL in the osteoporotic group were statistically significant ($P < 0.05$). Logistic multivariate regression analysis showed that lower extremity vascular sclerosis was an independent risk factor for osteoporosis in elderly men with type 2 diabetes mellitus ($P < 0.05$). **Conclusion:** Atherosclerosis of the lower extremities in elderly men with T2DM is closely related to osteoporosis, and can lead to a decrease in bone mass, and an increase in osteoporosis.

Keywords

Elderly Men with Type 2 Diabetes Mellitus, Lower Extremity Atherosclerosis, Osteoporosis

1. Introduction

Type 2 diabetes is the most common type of diabetes, accounting for 90% - 95%

of all the patients with diabetes, and the number of patients with Type 2 diabetes is expected to reach 439 million by 2030 [1]. The prevalence of diabetes increases with age. Among elderly people aged 60 to 74, 29.9% have diabetes and 36.85% are considered prediabetes, so the total prevalence of diabetes and prediabetes accounts for 66.7% in total [2]. In addition, the incidence of diabetic complications has been increasing in adults over the age of 65. For example, people with type 2 diabetes are 17 times more likely to have an amputation due to vascular atherosclerotic disease than non-diabetic patients, and are at an increased risk of developing osteoporotic disease [2]. Atherosclerosis will lead to arteries throughout the body, leading to hardening and thickening of the arterial walls, making the ABI an important indicator for assessing arterial atherosclerosis in the lower extremities [3].

There is a close and complex relationship between type 2 diabetes and osteoporosis. Studies proved that there is an association between the incidence of osteoporosis and type 2 diabetes [4]. In 2000, there were approximately 9 million osteoporotic fractures combined with diabetes worldwide [4]. The incidence of fractures increases with age. In the first year after a hip fracture, the mortality rate is 36% in men and 21% in women. The number of patients with osteoporosis in the first year after a hip fracture is estimated to be 1.5 million. In certain groups of patients, such as those with psychosis or other mental disorders, the mortality rate is reported to be higher than 50%. If patients survive a fracture, they will go through even harder challenges and are at a risk of permanent disability [5]. Osteoporosis is usually recognized as a typical disease for menopausal women, but recent data suggest that it is also progressively more common to see in elder men with type 2 diabetes [6]. Worldwide, osteoporosis and atherosclerosis of the lower extremity are prevalent in both sexes [4]. Some studies point to an age-dependent relationship, but there is no significant association between osteoporosis and lower extremity atherosclerosis [7]; other data show an association between osteoporosis only in menopausal women [8], but fewer studies have examined the relationship between osteoporosis and lower extremity vascular atherosclerosis in older men with type 2 diabetes mellitus [9]. We need to do in-depth research in this area. It will provide new ideas for diagnosis and treatment.

2. Materials and Methods

2.1. Clinical Data

359 patients of elderly men with diabetes mellitus were hospitalized in the First Affiliated Hospital of Chongqing Medical University from January 2018 to June 2023 were selected, with the minimum age of 60 years old, the maximum age of 95 years old, and the average age of (70.70 ± 7.97) years old. All patients signed an informed consent form. The study protocol was evaluated and validated by the hospital ethics committee. According to the T value, 248 patients were categorized into the osteoporosis group ($T \leq -2.5$) and 111 patients were categorized into the non-osteoporosis group ($T > -2.5$).

2.2. Diagnostic Criteria

Diagnostic Criteria DM refers to the relevant diagnostic criteria of the "Chinese Guidelines for the Prevention and Control of Type 2 Diabetes Mellitus (2023 Edition)". Clinical symptoms: polydipsia, polyuria, weight loss with unknown cause; the random blood glucose was ≥11.1 mmol/L, the fasting (for 8 hours) blood glucose was ≥7.0 mmol/L; the blood glucose result of 2-hour oral glucose tolerance test (OGTT) was ≥11.1 mmol/L.

2.3. Inclusion Criteria

1) All patients were over 60 years old;
2) All patients were male;
3) All patients had type 2 diabetes;
4) Patients were willing to complete and cooperate with the examination;
5) All knew and were willing to participate in this study.

2.4. Exclusion Criteria

1) Type 1 diabetes mellitus and other special types of diabetes mellitus;
2) Hemiplegia, braking and long-term bed-ridden;
3) Other diseases that affect bone metabolism, such as thyroid disease, parathyroid disease, adrenal disease, gonadal disease, rheumatoid arthritis, liver and kidney disease, metabolic bone disease, etc.;
4) Various other cancers;
5) Recent major surgery, serious infections, trauma, and other stressful conditions;
6) Have taken various kinds of hormones such as glucocorticoids, estrogens, fluoride and other drugs that affect bone metabolism.

2.5. Research Methods

2.5.1. Observation Indexes

Age, gender, duration of diabetes, height, weight, body mass index (BMI), smoking history, systolic blood pressure, diastolic blood pressure.

Biochemical parameters: Total cholesterol, triglyceride, high-density lipoprotein (HDL), low-density lipoprotein (LDL), all parameters should be measured by automatic biochemical analyzers.

2.5.2. Bone Densitometry

Dual-energy X-ray bone densitometry was used to detect the bone density of the patient's left hip and L1 - L4 lumbar vertebrae, and the low values were taken for analysis. Osteoporosis was diagnosed according to the Interpretation of the 2023 Edition of Clinical Guidelines for Prevention and Treatment of Osteoporosis. Osteoporosis: $T \leq -2.5$, Bone loss: $-2.5 < T < -1.0$, Normal bone mass: $T \geq -1.0$.

2.5.3. Measurement of Ankle-Brachial Index (ABI)

The ratio of systolic blood pressure at both ankles (dorsal foot artery or posterior tibial artery) to brachial artery was measured by doppler ultrasound at resting

and lying flat. ABI on both sides was calculated respectively, and the lower value was taken for analysis. The patients were divided into 2 groups according to the ratio of ankle-brachial index, the ABI < 0.9 group and the ABI ≥ 0.9 group. Patients with ankle-brachial index > 1.3 were excluded.

2.6. Statistical Analysis

SPSS 26.0 statistical software was used for data processing. The measurement data were represented by mean ± standard deviation, and T-test was used for comparison between groups. Counting data were expressed as cases and percentages, and Chi-square test was used to compare differences. Multivariate Logistic regression analysis of independent risk factors for type 2 diabetes in elderly men and the difference was considered statistically significant at $P < 0.05$.

3. Results

3.1. Comparison of Patients' General Information

359 elderly male patients with type 2 diabetes mellitus were included in this study, including 111 in the osteoporosis group, accounting for 30.92%, and 248 in the non-osteoporosis group, accounting for 69.08%. The duration of diabetes (years), systolic blood pressure, ABI, and BMI of patients in the osteoporosis group were significantly different from those in the non-osteoporosis group (all $P < 0.05$). There was no statistically significant difference in age and smoking between the two groups (all $P > 0.05$), see Table 1.

Table 1. Comparison of general information of the two groups of cases.

item	Osteoporosis (n = 111)	Nonosteoporosis (n = 214)	T	P
age (year)	71.59 ± 8.34	70.29 ± 7.78	−1.311	0.190
**Diabetes course* (year)	11.20 ± 7.53	13.64 ± 7.15	−3.002	0.003
Smoking history				
yes (case)	77 (69.4%)	179 (72.2%)	0.209	0.587
no (case)	34 (30.6%)	69 (27.8%)		
**ABI*				
ABI < 0.9 (case)	15 (13.5%)	13 (5.2%)	7.296	0.007
ABI ≥ 0.9 (case)	96 (86.5%)	235 (94.8%)		
**BMI* (kg/m^2)	23.10 ± 3.60	24.15 ± 3.60	−4.059	0.001
**hypertension* (mmHg)				
(*SBP* ≥ 140 *or DBP* ≥ 90)			5.179	0.023
yes (case)	46 (41.4%)	135 (54.4%)		
no (case)	65 (58.6%)	113 (45.6%)		

Note: Comparing the two groups, *P < 0.05.

3.2. Comparison of Biochemical Indexes between the Two Groups

The levels of uric acid (μmol/L), triglyceride (mmol/L), high-density lipoprotein (mmol/L) and uric acid (mmol/L) in osteoporosis group were higher than those in non-osteoporosis group, and the differences were statistically significant ($P < 0.05$). There were no significant differences in total cholesterol, low density lipoprotein, blood calcium, blood magnesium and blood phosphorus ($P > 0.05$) (Table 2).

3.3. Correlation between Atherosclerosis of Lower Extremity Vessels and Osteoporosis in Patients with Type 2 Diabetes Mellitus

Indicators with statistical differences in univariate analysis, such as diabetes duration (year), systolic blood pressure, ABI, BMI, blood uric acid (μmol/L), triglyceride (mmol/L) and high-density lipoprotein (mmol/L), were included in multi-factor Logistics regression analysis. The results showed that ABI was an independent risk factor for osteoporosis in elderly men with type 2 diabetes ($P < 0.05$). There was little correlation between uric acid and diabetes course (Table 3).

4. Discussion

For more than a century, clinicians have observed that osteoporosis often occurs

Table 2. Comparison of laboratory indicators between the two groups.

	Osteoporosis (n = 111)	Nonosteoporos (n = 248)	T	P
**Uric acid* (μmol/L)	307.11 ± 122.00	341.50 ± 121.75	−3.569	0.001
calcium (mmol/L)	2.27 ± 0.18	2.30 ± 0.17	−1.490	0.136
magnesium (mmol/L)	0.80 ± 0.12	0.81 ± 0.12	−0.227	0.820
phosphorus (mmol/L)	1.16 ± 0.25	1.15 ± 0.26	−0.029	0.977
TC (mmol/L)	3.82 ± 1.37	3.68 ± 1.35	−0.539	0.590
**TG* (mmol/L)	1.15 ± 0.72	1.22 ± 1.10	−2.207	0.027
**HDL* (mmol/L)	1.09 ± 0.36	1.00 ± 0.36	−2.235	0.025
LDL (mmol/L)	2.22 ± 1.18	2.17 ± 1.17	−0.067	0.946

Note: Comparing the two groups, *P < 0.05.

Table 3. Multifactorial logistics regression analysis of combined osteoporosis in elderly men with type 2 diabetes mellitus.

	β	SE	OR	95% CI	P
ABI < 0.9 (*case*)	0.653	0.278	1.922	1.115 - 3.314	0.019
Uric acid (μmol/L)	−0.003	0.001	0.997	0.995 - 0.999	0.011
Diabetes course (year)	−0.027	0.013	0.974	0.949 - 0.999	0.046

in elderly male patients with type 2 diabetes mellitus complicated with arteriosclerosis of lower limbs [10]. Studies have found that compared with non-T2DM patients, T2DM patients have a higher proportion of osteoporosis and lower extremity atherosclerosis, and T2DM patients with lower extremity arteriosclerosis often have fractures [10]. This indicates that blood glucose level may have some relationship with the above two diseases, and it is also suggests that there may be a certain correlation between lower limb atherosclerosis and osteoporosis [10]. It has been suggested that there is a common reason of type 2 diabetes, osteoporosis and atherosclerotic disease of the lower extremity vasculature [4]. On the one hand, the decrease of bone density may be related to inflammation, and one of the possible factors is involved in the inflammatory signal transmission process mediated by interleukin-6 (IL-6) [4]. IL-6-mediated inflammatory response is common in patients with atherosclerosis of lower extremity vasculature as well as in patients with type 2 diabetes mellitus [11]. Vascular atherosclerosis is the most common, and vascular sclerosis seems to be caused by the osteogenic differentiation of vascular cell subsets induced by inflammatory factors, such as modified lipoprotein [12]. This suggests a correlation between vascular sclerosis and bone metabolism [12]. On the other hand, the decrease of bone mineral density may be related to abnormal blood glucose. Hyperglycemia will cause osmotic diuresis, lead to a large loss of phosphorus and calcium, and the levels of blood phosphorus and blood calcium will continue to decrease, thus causing bone loss and increasing the incidence of osteoporosis [13]. Long-term hyperglycemia will cause non-enzymatic glycosylation of bone proteins, and the increasing advanced glycation end products (AGEs) will induce the production of various cytokines and adhesion molecules by acting on monocytes and smooth muscle cells. This will stimulate the occurrence of inflammatory reaction, further damage the function of endothelial cells, and eventually lead to the proliferation of smooth muscle cells and accelerate the formation of atherosclerosis. Excessive glycosylation may reduce bone mass [14]. Animal experiments show that glycosylation can induce the increase of non-enzymatic cross-linking substances in bones, which will damage the biomechanical properties of bones and increase the risk of osteoporosis [14].

T2DM patients are often accompanied by insulin resistance, and insulin resistance and hyperinsulinemia will increase the risk of arteriosclerosis and bone loss in lower limbs [15]. First of all, insulin resistance can destroy the function of vascular endothelial cells, lead to increased lipid deposition [16], and then accelerate the formation of atherosclerosis; Secondly, due to the lack of insulin, it is difficult to combine with insulin receptor, and it cannot play a normal role in lowering blood sugar, which will stimulate the synthesis of osteoblasts, resulting in a decline in bone mass [17].

At present, it has been reported that statins can play a dual role in anti-atherosclerosis and increasing bone mineral density [11]. Of course, there are other factors affecting osteoporosis in elderly men, such as vitamin D metabolism disorder and androgen level, which are also related to lower extremity atherosclero-

sis [17] [18] [19]. However, because this study is only a preliminary discussion on the correlation between the two diseases, the above indicators have not been detected and evaluated, which needs to be further discussed in the future.

The results of this study show that the incidence of lower extremity atherosclerosis in elderly men with type 2 diabetes mellitus is significantly higher than that in non-osteoporosis group. At the same time, in the atherosclerotic population, the decline of bone mineral density is more obvious with the aggravation of atherosclerosis. This shows that after excluding confounding factors, the study still shows that atherosclerosis of lower limbs is related to osteoporosis. The results of this study suggest that lower extremity atherosclerosis in elderly male patients with T2DM is closely related to osteoporosis, and lower extremity atherosclerosis can cause bone loss and increase the possibility of osteoporosis. However, limited by the research conditions, the case selection lacks randomness, the sample size is small, and the influence mechanism of some factors is not thoroughly analyzed. Therefore, the relationship between lower extremity arteriosclerosis and osteoporosis in elderly male patients with type 2 diabetes needs further study, which may bring new ideas to the prevention and treatment of osteoporosis and lower extremity arteriosclerosis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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