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·临床研究·

2型糖尿病合并骨质疏松相关因素的分析

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摘要:目的 探讨2型糖尿病合并骨质疏松的相关因素,并为进一步治疗提供相关依据。**方法** 2型糖尿病患者157例,男性79例,女性78例,其中分为合并骨质疏松组(OP)74例,未合并骨质疏松组(NOP)83例。分析比较这两组患者的性别、年龄、病程、体重指数(BMI)、血钙(Ca)、血磷(P)、碱性磷酸酶(ALP)、空腹血糖(FBG)、糖化血红蛋白(HBA1c)、尿微量白蛋白、血肌酐、甘油三酯(Tg)、总胆固醇(Tc)、高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)、25羟基维生素D的差异。**结果** 骨质疏松组与非骨质疏松组比较,性别、病程、BMI、HBA1c、血肌酐、尿微量白蛋白、25羟基维生素D有统计学差异性($P<0.05$),而Ca、P、ALP、FBG、Tg、Tc、HDL-C、LDL-C无统计学意义($P>0.05$);二元Logistic回归分析显示病程、BMI、HBA1c、25羟基维生素D与OP有关。**结论** 病程、BMI、HBA1c、25羟基维生素D是影响2型糖尿病合并骨质疏松的相关因素。

关键词: 2型糖尿病;骨质疏松;25羟基维生素D;相关因素

Risk factors of osteoporosis in type 2 diabetic patients

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Abstract: Objective To investigate the risk factors of osteoporosis in type 2 diabetic patients and to provide the guidance for the further treatment. **Methods** One hundred and fifty-seven type 2 diabetic patients (79 males and 78 females) were enrolled in the study, including 74 cases complicated with osteoporosis and 83 cases without osteoporosis. The clinical data (age, sex, BMI, and course of disease) and laboratory parameters (Ca, P, ALP, FBG, HbA1c, mAlb, SCr, LDL-C, HDL-C, 25(OH)D, Tc, and Tg) were compared between the two groups. **Results** The sex, course of disease, BMI, HbA1c, mAlb, SCr, and 25(OH)D were significantly different between patients with osteoporosis and without osteoporosis ($P<0.05$). However, Ca, P, ALP, FBG, Tg, Tc, HDL-C, and LDL-C were not different between the two groups. Logistic regression analysis revealed that longer course of disease, higher HBA1c, lower 25(OH)D, and lower BMI were correlated with osteoporosis. **Conclusion** The influential factors of osteoporosis in type 2 diabetic patients are course of disease, HBA1c, 25(OH)D, and BMI.

Key words: Type 2 diabetes; Osteoporosis; 25(OH)D; Influential factors

1948年Albright首次提出糖尿病可致骨改变后,糖尿病继发引起的骨质疏松越来越得到人们的重视。糖尿病继发骨质疏松的发病率为50%~60%[1]。目前认为T1DM可降低骨密度[2,3],导致骨质疏松已得到明确的肯定。虽然2型糖尿病对骨密度的影响,目前结论不统一,可正常、低于正常或高于正常[4],但是2型糖尿病较易合并骨质疏松[5]。本文为研究2型糖尿病合并骨质疏松的相关因素,进一步指导骨质疏松的预防与治疗。

1 资料与方法

1.1 一般资料

江苏省中医院2015年3月—2015年11月的内分泌科住院患者,均符合根据1999年WHO为标准确诊的2型糖尿病;骨质疏松(OP)的诊断均参照按世界卫生组织(WHO)推荐的骨质疏松诊断标准,即

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绝经后妇女和大于50岁男性的骨密度水平用T值表示，儿童、绝经前妇女以及小于50岁男性的骨密度水平用Z值表示。将T值或Z值≥-1.0者为骨量正常，-2.5<T值或Z值<-1.0者为骨量减少，将T值或Z值≤-2.5者为骨质疏松[6]。所有患者半年内均无服用糖皮质激素类药物的病史；并排除垂体、甲状腺、甲状旁腺、肾上旁腺、肾上腺、性腺及肿瘤等疾病；无长期卧床者；无合并严重心、肺、肾等器官疾病者。

1.2 方法

测量、统计患者的姓名、年龄、性别、糖尿病病程、身高、体重等相关临床资料，并计算体重指数(BMI)：BMI=体重(kg)/身高^2(m^2)。使用美国HOLOGIC双能X线骨密度仪进行非优势侧股骨近端、髋部和腰椎的骨密度测定，用全自动生化分析仪测定空腹血糖、血钙、血磷、碱性磷酸酶(ALP)、血肌酐、甘油三酯(Tg)、总胆固醇(Tc)、高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)、尿微量白蛋白，用高压液相法测定糖化血红蛋白(HBA1c)，化学发光法测25羟基维生素D。

1.3 统计学处理

统计学方法数据通过SPSS19.0统计软件进行分析，计量资料的比较用$\bar{x}\pm s$表示，均进行正态分布检验，组间比较采用独立样本t检验法，用二元Logistic回归分析2型糖尿病与OP的相关影响因素，$P<0.05$具有统计学差异。

2 结果

2.1 临床资料(见表1)

2型糖尿病患者共157例，男79例，女78例；T2DM合并OP组74例，男30例，女44例，年龄(62.39±12.06)岁，病程(12.42±6.64)年，BMI(23.40±2.79)kg/m^2；T2DM合并NOP组83例，男49例，女34例，年龄(61.37±10.79)岁，病程(9.64±5.95)年，BMI(26.27±3.85)kg/m^2；T2DM合并OP组病程较长($P<0.05$)、BMI较小($P<0.05$)，年龄差别较小($P>0.05$)。

2.2 实验数据资料(见表2,3)

T2DM合并OP组较未合并OP组患者25羟基维生素D偏低($P<0.05$)、HBA1c偏高($P<0.05$)、尿微量白蛋白偏高($P<0.05$)、血肌酐偏高($P<0.05$)、女性比例较大；其他实验数据差异无统计学意义，P值均大于0.05。

表1 NOP组与OP组临床资料的比较

Table 1 Comparison of general clinical data between OP group and NOP group

组别	男/女	年龄(岁)	病程(年)	BMI(kg/m^2)
T2DM合并NOP	49/34	61.37±10.79	9.64±5.95	26.27±3.85
T2DM合并OP	30/44	62.39±12.06	12.42±6.64*	23.40±2.79*

注：*与合并NOP组比较，$P<0.05$

表2 NOP组与OP组实验数据比较(第一部分)

Table 2 Comparison of the laboratory results between OP and NOP (Part 1)

组别	FBG(mmol/L)	Ca (mmol/L)	P (mmol/L)	ALP (U/L)	Tg (mmol/L)	Tc (mmol/L)
T2DM合并NOP	8.36±5.13	2.25±0.13	1.09±0.17	104.90±28.93	1.56±1.06	4.33±1.05
T2DM合并OP	8.13±2.47	2.29±0.18	1.07±0.16	106.16±36.88	1.34±0.66	4.31±0.94

表3 NOP组与OP组实验数据比较(第二部分)

Table 3 Comparison of the laboratory results between OP and NOP (Part 2)

组别	LDL-C (mmol/L)	HDL-C (mmol/L)	25羟基维生素D (nmol/L)	HbA1c (%)	尿微量白蛋白 (mg/L)	血肌酐 (μmol/L)
T2DM合并NOP	2.44±0.64	1.21±0.31	50.24±20.72	8.49±1.63	50.01±84.44	60.52±26.88
T2DM合并OP	2.39±0.68	1.19±0.35	36.59±15.56*	9.80±1.95*	103.51±221.25*	67.67±14.31*

注：*与合并NOP组比较，$P<0.05$

2.3 T2DM合并OP中影响因素的相关性(表4)

二元Logistic回归分析显示，把T2DM合并OP作为因变量，性别(设男为0，女为1)、病程、尿微量白蛋白、血肌酐、25羟基维生素D、HBA1c、BMI作为

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自变量，病程、25羟基维生素D、HBA1c、BMI与T2DM合并OP相关见表4。

表4 2型糖尿病合并骨质疏松影响因素

Table 4 Risk factors of osteoporosis in type 2 diabetic patients

项目	B	Wals	OR	95% CI	P
病程	0.071	4.488	1.073	1.005 - 1.146	0.034
25羟基维生素D	-0.042	10.907	0.959	0.935 - 0.983	0.001
HbA1c	0.323	7.165	1.382	1.090 - 1.751	0.007
尿微量白蛋白	0.001	0.446	1.001	0.998 - 1.004	0.504
BMI	-0.275	13.915	0.760	0.658 - 0.878	0.000
性别	-0.645	2.470	0.525	0.235 - 1.173	0.116
血肌酐	0.012	1.619	1.012	0.994 - 1.031	0.203

3 讨论

骨质疏松症(osteoporosis, OP)是以骨量减少、骨质微结构破坏导致的骨脆性增加和易于骨折的代谢性骨病。骨质疏松症可分为原发性和继发性两型。继发性骨质疏松症是可以找到明确病因的一类骨质疏，临床上可分为内分泌代谢病、结缔组织病、肾脏疾病、消化道疾病和药物所致等。但原发性骨质疏松往往合并有继发性骨质疏松，或继发性骨质疏松涉及多种危险因素，糖尿病继发性骨质疏松就是属于这一类。T2DM患者代谢性骨病的发病率和骨质疏松骨折的危险性明显高于普通人群，其骨质疏松的发生率可达20% ~60%[7]。

糖尿病患者长期的高血糖引起高渗状态导致渗透性利尿，促进钙、磷的排出，抑制钙磷的重吸收，低钙又会刺激甲状旁腺激素的分泌，高血糖可致成骨细胞对甲状旁腺激素敏感性降低[8]，最终引起甲状旁腺激素升高动员骨钙入血，引起骨密度降低；糖尿病病程越长，高渗状态的毒性越大，引起骨质疏松的风险也越大，2型糖尿病患者的病程与骨矿的丢失有关[9]，2型糖尿病初发期的骨密度与正常人相比无明显改变[10]的报道与本研究相一致；长期的高血糖，会逐渐形成糖基化终末产物，促进IL-1、IL-6、TGF-α等细胞因子的释放，导致骨质疏松[11]；糖化血红蛋白反应了既往3个月左右血糖的控制状况，本研究中糖化血红蛋白偏高也是骨质疏松的一个危险因素，也吻合了长期的高血糖对骨质疏松的影响。糖尿病病变影响肾脏时，可使肾脏合成1,25(OH)$_2$D$_3$减少，肠道吸收钙减少，继发性引起甲旁亢，形成骨质疏松，在糖尿病肾病晚期，长期代谢性酸中毒，增加骨钙入血，骨矿化收到影响，加重骨质疏松；在组间比较时尿微量白蛋白及血肌酐为骨质疏松的影响因素，相关因素分析时，相关性无统计学意义，这可能与所选病例中糖尿病对肾脏的影响不是很明显或只是达到轻度水平。糖尿病患者长期口服降糖药物对骨质疏松也有影响，噻唑烷二酮类药物可导致糖尿病患者骨密度下降[12]及TZDs对骨代谢有不良反应，表现为骨量流失或骨折[13-14]。

本研究表明BMI为糖尿病合并骨质疏松的独立危险因素，与骨质疏松呈负相关，很多研究也表明肥胖与骨矿密度(BMD)正相关，对预防骨质疏松症发生有保护性作用，降低骨折风险[15,16]；这可能是高BMI时增加骨骼所承受的机械负荷，增加骨骼应力，刺激骨形成，增加骨的强度，减少骨质疏松的发生。女性发生骨质疏松的比例比男性大，与男性相比，女性T2DM患者更易发生骨质疏松[17-19]，这可能与更年期后女性雌激素骤减相关。

血清25羟基维生素D是维生素D在体内的主要存在形式，是目前公认的评价维生素D营养状况的金指标[20]，基本生理功能是调节钙磷代谢。维生素D主要通过以下途径调节钙磷代谢：(1)促进肠钙的吸收；(2)抑制PTH的合成和分泌；(3)促进破骨细胞前体细胞分化为破骨细胞，故促进骨吸收，同时也促进Ⅰ型胶原和骨钙素的合成。因此25羟基维生素D有促进骨形成和抑制骨吸收的作用[21]。2型糖尿病患者的血清1,25(OH)2D$_3$水平倾向比正常人群偏低[22-24]，偏低的原因可能是2型糖尿病患者血清25羟基维生素D水平降低与胰岛素抵抗增加及胰岛β细胞功能降低有关[25]，低维生素D水平也是发生胰岛素抵抗和代谢综合征的危险因素[26,27]，另一方面维生素D又可增加机体组织对胰岛素敏感性[28]。因此低维生素D水平既可增加糖尿病相关风险，又增加骨质疏松的风险性。血清25羟基维生素D低水平可能是2型糖尿病合并骨质疏松的高危因素之一[29]。年龄大者2型糖尿病更容易合并骨质疏松[30,31]，而更容易引起维生素D水平的缺乏[32]，本研究与年龄无相关性，可能与所选患者的年龄普遍偏大有关。

综上所述，有多重因素影响2型糖尿病合并骨质疏松，这些影响因素相互交织，其中糖尿病病程长、BMI低、血糖控制不佳(HbA1c高)、维生素D水平低是2型糖尿病合并骨质疏松的危险因素。维生素D及钙剂为骨质疏的基础治疗，在骨质疏松的基础治疗及预防中，合理补充维生素D，不仅能增加胰岛素的敏感性，减少骨质疏松的风险，还能增强免疫力[33]，积极控制血糖，增强锻炼及适当增加体重可

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预防2型糖尿病合并骨质疏松及骨质疏松性骨折的发生风险。

中医药在骨质疏松的治疗中亦有其独到的优势。中医学认为,本病的发生主要与肾虚、脾虚、血瘀等因素有关,就脾肾亏虚为本,血瘀为标是骨质疏松症的病理特点[34]。针对不同骨质疏松辩证分型,中医的治法不同,有健脾补肾[35]等,在此治法的基础上立方的方剂有健骨丸[36]等在临床的运用中已经取得了很大的成功。中医药治疗骨质疏松有多靶点、副作用少的明显优势,不仅抑制破骨细胞的骨吸收,还能促进成骨细胞的活性,从而达到骨吸收与骨形成的动态平衡,增强骨密度及骨强度。因此,在补充维生素D和补钙的基础治疗上,合理运用中医药治疗骨质疏松亦有很大的进展及临床疗效。

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万方数据

给不足,产生不良反应。因此外源性补充辅酶 Q_{10} 可避免他汀类引起的不良反应,并能增强他汀的抗骨丢失作用。因此,补充含辅酶 Q_{10} 和洛伐他汀的红曲提取物可降低大鼠胆固醇的水平,具有减轻体重作用,由于其直接抵抗破骨作用,对成骨作用影响不大,因此在一定程度上可抗骨丢失,但长期应用对骨代谢的影响还有待下一步探究。

3月龄的SD大鼠双侧去卵巢后,每天皮下注射D-半乳糖 100 $mg \cdot kg^{-1} \cdot d^{-1}$,60天后,大鼠体重增加,胫骨松质骨骨量丢失严重,骨显微结构严重退化,胫骨皮质骨的面积减少,可造成老年性骨质疏松。给予0.5颗·$kg^{-1} \cdot d^{-1}$含辅酶 Q_{10} 和洛伐他汀的红曲提取物胶囊后,大鼠体重明显减轻,胫骨松质骨以及胫骨皮质骨的骨丢失明显减轻,提示该天然提取物具有减肥及防治骨质疏松的良好应用前景。

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