

• 临床研究 •

## 绝经后 2 型糖尿病患者血脂与骨代谢的关系

征海华 雷涛 江东梅 戚蓓蓓 宋文春

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**摘要:** 目的 探讨绝经后 2 型糖尿病患者血脂与骨代谢的相关性。方法 将 300 例绝经后 2 型糖尿病患者按 T 值分成骨质疏松组和非骨质疏松组;检测两组患者血清总胆固醇(TC)、甘油三酯(TG)、高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)及骨代谢指标,分析血脂各成分与骨代谢之间的关系。结果 (1) 绝经后 2 型糖尿病患者的 HDL-C 与 OT、TrACP、uNTX/Cr 存在正相关( $r_1 = 0.134, P_1 = 0.020; r_2 = 0.181, P_2 = 0.002; r_3 = 0.126, P_3 = 0.030$ ),与 BALP 无相关性;TC 与 TrACP 呈负相关( $r = -0.153, P = 0.038$ ),与 OT、BALP、uNTX/Cr 无相关性;TG、LDL-C 与 OT、BALP、TrACP、uNTX/Cr 均无相关性。(2) 在校正年龄、绝经年限和 BMI 影响因素后,HDLC 与 TrACP、uNTX/Cr 仍存在正相关( $r_1 = 0.160, P_1 = 0.010; r_2 = 0.125, P_2 = 0.045$ ),而 HDLC 与 OT、TC 与 TrACP 间的相关性失去统计学意义。结论 绝经后 2 型糖尿病患者的 HDL-C 与 TrACP、uNTX/Cr 存在正相关,与 OT、BALP 无相关性;而 TC、TG、LDL-C 与 OT、BALP、TrACP、uNTX/Cr 无明显相关性。

**关键词:** 血脂; 骨质疏松; 骨代谢; 2 型糖尿病; 绝经后

The relationship between serum lipid level and bone metabolism in postmenopausal women with type 2 diabetes ZHENG Haihua, LEI Tao, JIANG Dongmei, et al. Department of Endocrinology, the Affiliated Tongji Hospital of Shanghai Tongji University, Shanghai 200065, China

Corresponding author: LEI Tao, Email:leitao5899@126.com

**Abstract:** Objective To investigate the correlation between the serum lipid level and bone metabolism in postmenopausal women with type 2 diabetes. Methods Three hundred postmenopausal women with type 2 diabetes were divided into osteoporosis group ( $T \leq -2.5$ ) and non-osteoporosis group ( $T > -2.5$ ) according to their T scores. The levels of serum total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and bone metabolism markers in the patients were determined. The correlation between serum lipids and bone metabolism markers were analyzed. Results (1) In postmenopausal women with type 2 diabetes, the HDL-C level was positively correlated with OT, TrACP, and uNTX/Cr ( $r_1 = 0.134, P_1 = 0.020; r_2 = 0.181, P_2 = 0.002; r_3 = 0.126, P_3 = 0.030$ ), but was not correlated with BALP. The TC level was negatively correlated with TrACP ( $r_1 = -0.153, P_1 = 0.038$ ), but was not correlated with OT, BALP, and uNTX/Cr. There were no relationships among TG, LDL-C levels and OT, BALP, TrACP, and uNTX/Cr. (2) After adjustment for age, menopause age, and BMI, the associations between HDL-C and TrACP, uNTX/Cr remained statistically significant ( $r_1 = 0.160, P_1 = 0.010; r_2 = 0.125, P_2 = 0.045$ ), while the association between HDL-C and OT, and between TC and TrACP lost the statistical significance. Conclusions The HDL-C level showed positive correlations with TrACP and uNTX/Cr, no correlations with OT and BALP in postmenopausal women with type 2 diabetes. There were no significant relationships among the TC, TG, LDL-C levels and OT, BALP, TrACP, and uNTX/Cr.

**Key words:** Serum lipid; Osteoporosis; Bone metabolism; Type 2 diabetes; Postmenopausal

作者单位: 224001 盐城, 东南大学附属盐城医院内分泌科(征海华、江东梅、戚蓓蓓、宋文春); 同济大学附属同济医院内分泌科(雷涛)

通讯作者: 雷涛, Email:leitao5899@126.com

随着人类生活水平的提高,生活方式的改变和社会人口的老龄化,骨质疏松症、动脉粥样硬化、糖尿病(DM)等疾病的发病率明显增高。研究发现骨质疏松与动脉粥样硬化可能存在共同的危险因子及流行病学改变,两者存在相似的局部细胞因子和细胞反应<sup>[1,2]</sup>。血脂紊乱是动脉粥样硬化的危险因素,但血脂紊乱与骨质疏松的相关性研究国内外学者结果不一<sup>[3-6]</sup>。2型糖尿病患者常伴有脂代谢紊乱,同时发生骨质疏松的风险也显著增加。特别是绝经后妇女,因为体内雌激素水平的减少,更容易发生骨质疏松<sup>[7-10]</sup>。故为排除血糖和激素水平的影响,选择在绝经后2型糖尿病人群中研究和探讨脂代谢紊乱和骨质疏松的关系,从而对该人群骨质疏松的防治提供新的理论依据和途径。

## 1 对象和方法

### 1.1 对象

选择2008年6月至2010年6月期间就诊于上海同济大学附属同济医院内分泌科绝经后2型糖尿病患者300例。符合下列标准:①绝经后女性:自然绝经大于等于5年;②符合1999年WHO制定的糖尿病诊断标准;③骨质疏松的诊断标准为:骨密度T值低于同性别BMD峰值平均值的2.5个标准差( $T \leq -2.5$ );④以上研究对象排除DM急性并发症、感染等应激状态;半年内未服用降脂、治疗骨质疏松以及影响骨代谢、脂代谢的药物(如噻唑烷二酮类、胰岛素、糖皮质激素等);排除肾脏、垂体、甲状腺、甲状旁腺、肾上腺和原发性腺等可能影响骨代谢的疾病;否认激素替代治疗(hormone replace treatment,HRT)史;非T<sub>1</sub>DM、其他特殊类型DM或妊娠DM。

### 1.2 分组

按上述骨质疏松诊断标准将受检对象分为骨质疏松组(OP)和非骨质疏松组(NOP);

### 1.3 方法

患者的一般情况:身高、体重,计算BMI;测量收缩压、舒张压;记录年龄、绝经年限;生化实验室指标检测方法:采用Beck MAN Coulter Unicel Dex 800 Synchron Clinical System全自动生成分析仪,测量空腹静脉血生化指标。血脂谱测定:血总胆固醇(TC)、甘油三酯(TG)采用酶法(GOD-PAPF法);高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)采用匀相测定法。血糖测定:空腹血糖(FBG)采用葡萄糖氧化酶法;糖化血红蛋白(HbA<sub>1c</sub>)应用高效液相色谱分析法。雌二醇(E<sub>2</sub>)

测定:采用化学发光法。肝功能测定:谷丙转氨酶(ALT)、谷草转氨酶(AST)采用连续检测法。肾功能测定:尿素氮(BUN)采用酶电导率法;肌酐(Cr)采用苦味酸法。血钙(Ca)采用间接电位法;血磷(P)采用磷钼酸法;25(OH)VD<sub>3</sub>采用ELISA;甲状腺激素(PTH)采用化学发光法;骨钙素(OT)采用电化学发光法;骨源性碱性磷酸酶(BALP)、抗酒石酸酸性磷酸酶(TrACP)、尿I型胶原交联氨基端肽与肌酐比值(uNTX/Cr)采用ELISA。

### 1.4 统计学处理

结果以( $\bar{x} \pm s$ )表示,采用SPSS 16.0软件进行统计学分析。组间均数差异符合正态分布用Student's t检验,偏态分布用非参数检验;骨代谢指标与其影响因素的相关性用Pearson's相关以及偏相关分析。 $P < 0.05$ 为有统计学差异, $P < 0.01$ 为有显著统计学差异。

## 2 结果

### 2.1 两组一般资料的比较

绝经后2型糖尿病患者OP组与NOP组相比,两组间年龄、绝经年限、BMI存在明显差异,OP组患者的年龄较大、绝经年限较长而BMI较低,结果见表1。

表1 绝经后2型糖尿病患者OP组与 NOP组一般资料的比较( $\bar{x} \pm s$ )

	OP组(147例)	NOP组(153例)
年龄(年)	72.59 ± 8.83	65.65 ± 11.42 **
绝经年限(年)	21.69 ± 7.86	17.26 ± 11.19 **
BMI(kg/m <sup>2</sup> )	21.79 ± 1.63	25.73 ± 2.03 *
收缩压(mmHg)	142.04 ± 11.61	140.08 ± 10.79
舒张压(mmHg)	84.07 ± 7.19	81.01 ± 6.50
FBG(mmol/L)	7.94 ± 1.98	7.70 ± 2.35
HbA <sub>1c</sub> (%)	7.68 ± 1.54	7.43 ± 1.39
E <sub>2</sub> (nmol/L)	0.065 ± 0.018	0.069 ± 0.016
GPT(U/L)	20.56 ± 19.95	21.70 ± 17.19
GOT(U/L)	21.56 ± 15.33	20.62 ± 13.98
BUN(mmol/L)	6.05 ± 6.29	5.45 ± 3.83
Cr(μmol/L)	60.52 ± 2.75	59.17 ± 2.36

注:骨质疏松组和非骨质疏松组比较 \* $P < 0.05$ , \*\* $P < 0.01$

### 2.2 两组血钙、磷及钙调节相关激素的比较

绝经后2型糖尿病患者OP组与NOP组相比,两组间血Ca、P、PTH差异无统计学意义,两组间25(OH)VD<sub>3</sub>有显著性差异,OP组25(OH)VD<sub>3</sub>明显降低,结果见表2。

**表2** 绝经后2型糖尿病患者OP组与NOP组血钙、磷及钙调节相关激素的比较( $\bar{x} \pm s$ )

	OP组(147例)	NOP组(153例)
Ca (mmol/L)	2.30 ± 0.46	2.27 ± 0.23
P (mmol/L)	1.29 ± 0.22	1.33 ± 0.24
25(OH)VD <sub>3</sub> (nmol/L)	30.91 ± 4.52	38.29 ± 9.93 **
PTH (pg/ml)	52.11 ± 6.67	51.71 ± 5.93

注:OP组和NOP组比较 \*P&lt;0.05, \*\*P&lt;0.01

**2.3 两组骨代谢指标及血脂的比较**

绝经后2型糖尿病患者OP组与NOP组相比,两组间骨代谢指标及血脂存在明显差异,其中OP组的OT、BALP、TrACP、uNTX/Cr较高,HDL-C较高;而TC、TG、LDL-C差异无统计学意义,结果见表3。

**表3** 绝经后2型糖尿病患者OP组与NOP组的骨代谢指标及血脂的比较( $\bar{x} \pm s$ )

	OP组(147例)	NOP组(153例)
OT (ng/ml)	21.94 ± 2.47	14.77 ± 3.05 *
BALP (μg/L)	20.68 ± 2.11	14.92 ± 2.49 *
TrACP (U/L)	4.04 ± 0.48	2.57 ± 0.56 *
uNTX/Cr (nm BCE)	76.01 ± 12.10	31.98 ± 9.54 **
TC (mmol/L)	5.10 ± 0.84	5.30 ± 0.86
TG (mmol/L)	1.90 ± 0.43	2.03 ± 0.46
HDL-C (mmol/L)	1.06 ± 0.33	0.96 ± 0.27 **
LDL-C (mmol/L)	3.39 ± 1.06	3.57 ± 0.93

注:OP组和NOP组比较 \*P&lt;0.05, \*\*P&lt;0.01

**2.4 骨代谢指标与影响因素的相关性**

绝经后2型糖尿病患者的年龄分别与OT、BALP、TrACP、uNTX/Cr呈显著正相关( $r_1 = 0.275, P_1 = 0.000; r_2 = 0.215, P_2 = 0.000; r_3 = 0.275, P_3 = 0.000; r_4 = 0.264, P_4 = 0.000$ );绝经年限分别与OT、BALP、TrACP、uNTX/Cr呈显著正相关( $r_1 = 0.254, P_1 = 0.000; r_2 = 0.202, P_2 = 0.001; r_3 = 0.249, P_3 = 0.000; r_4 = 0.253, P_4 = 0.000$ );BMI分别与OT、BALP、TrACP、uNTX/Cr呈显著负相关( $r_1 = -0.564, P_1 = 0.000; r_2 = -0.573, P_2 = 0.000; r_3 = -0.562, P_3 = 0.000; r_4 = -0.681, P_4 = 0.000$ );TC与TrACP呈负相关( $r = -0.153, P = 0.038$ );HDL-C与OT呈正相关( $r = 0.134, P = 0.020$ ),与TrACP呈显著正相关( $r = 0.181, P = 0.002$ ),与uNTX/Cr呈正相关( $r = 0.126, P = 0.030$ ),结果见表4。

**2.5 血脂与骨代谢指标的相关性**

在校正年龄、绝经年限和BMI影响因素后,绝

经后2型糖尿病患者的HDL-C与TrACP、uNTX/Cr仍存在正相关( $r_1 = 0.160, P_1 = 0.010; r_2 = 0.125, P_2 = 0.045$ ),而HDL-C与OT、TC与TrACP间的相关性失去统计学意义,结果见表5。

**表4** 绝经后2型糖尿病患者骨代谢指标

## 与影响因素的相关性

变量	OT	BALP	TrACP	uNTX/Cr
年龄	0.275 **	0.215 **	0.275 **	0.264 **
绝经年限	0.254 **	0.202 **	0.249 **	0.253 **
BMI	-0.564 **	-0.573 **	-0.562 **	-0.681 **
TC	-0.094	-0.116	-0.153 *	-0.093
TG	-0.050	-0.117	-0.056	-0.093
HDL-C	0.134 *	0.104	0.181 **	0.126 *
LDL-C	-0.009	-0.089	-0.093	-0.074

注: \*P&lt;0.05, \*\*P&lt;0.01

**表5** 绝经后2型糖尿病患者血脂与骨代谢指标

## 的相关性(校正年龄、绝经年限、BMI)

变量	OT	BALP	TrACP	uNTX/Cr
TC	-0.040	-0.071	-0.099	-0.011
TG	0.055	-0.045	0.014	0.027
HDL-C	0.103	0.059	0.160 **	0.125 *
LDL-C	0.068	-0.059	-0.066	-0.016

注: \*P&lt;0.05, \*\*P&lt;0.01

**3 讨论**

目前骨质疏松症、动脉粥样硬化、糖尿病的发病人数逐年增加,流行病学研究发现动脉粥样硬化患者常伴有骨质疏松症,血脂紊乱是动脉粥样硬化的危险因素,而血脂紊乱与骨质疏松的相关性研究结果不一。本实验旨在进一步了解血脂对骨质疏松的影响,同时为排除血糖、激素水平对研究结果的影响,全部选择绝经5年以上的2型糖尿病患者。

本试验将绝经后2型糖尿病患者按是否合并骨质疏松分为两组,对比分析显示OP组的HDL-C、OT、BALP、TrACP、uNTX/Cr较NOP组明显增高,表明骨质疏松组存在着更为明显的脂代谢、骨代谢紊乱。脂质如何影响到骨质疏松的发生,这可能由于其影响到骨髓的分化,体外实验已证实脂蛋白氧化产物可促进骨髓干细胞向破骨细胞分化,而抑制其向成骨细胞分化<sup>[11,12]</sup>。另外他汀类降脂药物对骨代谢的影响则从侧面证实了血脂和骨代谢之间的密切关系。Rejnmark等<sup>[13]</sup>对140例服用他汀类药物2年的绝经后女性和140对照组的横断性研究发现:他汀类药物服用组的OT、BALP、CTX较对照组

明显降低。Parhami 等<sup>[14]</sup>研究进一步认为甲羟戊酸途径不仅是胆固醇合成的关键步骤,同时还可以调节骨细胞的增殖和凋亡。HMG-CoA 还原酶抑制剂能抑制骨髓干细胞向成骨细胞分化成熟。

本试验采用相关性分析进一步了解脂代谢与骨代谢间的具体关系,结果显示绝经后 2 型糖尿病患者的 HDL-C 与 TrACP、uNTX/Cr 存在正相关,与 OT、BALP 无相关性;而 TC、TG、LDL-C 与 OT、BALP、TrACP、uNTX/Cr 无明显相关性。提示 HDL-C 起着更为重要的作用,这可能因为 HDL-C 和脂肪量直接相关,脂肪组织较肌肉组织的机械刺激作用弱,影响骨皮质内外的骨重建,致使骨量、骨结构参数均下降。而目前国内的相关临床研究结论不一。Majima 等<sup>[15]</sup>将高胆固醇血症患者按照性别分成男、女两组后分析骨代谢指标与血脂的相关性,结果显示男性组患者 BAP、NTX 和 HDL-C 呈显著负相关,女性组患者 BAP、NTX 和 TC、LDL-C 呈显著正相关。童培建等<sup>[16]</sup>通过诱导激素性股骨头坏死的动物模型,观察分析脂质代谢及破骨细胞活性在激素性股骨头坏死塌陷发生过程中的作用,结果发现实验组的 TC、TG 及 TrACP 含量显著升高,其间且有显著相关性。然而,Hernández 等<sup>[17]</sup>的一项对 289 例西班牙白种男性进行研究,并没有发现 TC、TG、HDL-C、LDL-C 与 PINP、β-CTX 间有显著相关性。可见血脂紊乱与骨代谢的关系仍存有争议。这可能受限于研究对象的种族、年龄、性别、基础疾病状态以及研究方法等。也可能与疾病本身有关,因为骨质疏松症常伴有骨髓微环境的退化,有学者认为血液中脂肪的堆积影响骨髓的微环境,它可以使骨间隙压力增多,骨髓腔内的血管受压迫,血窦面积减少,血液供应不足,最终导致骨量丢失,所以高脂血症时骨髓腔内微循环障碍可能是造成骨质疏松的原因之一<sup>[18]</sup>。此外,因血脂紊乱是动脉粥样硬化的危险因素之一,动脉粥样硬化过程中释放较多的炎症因子和脂肪因子可能对骨质疏松的发生发展起着更为重要的作用<sup>[19]</sup>。在统一的内环境中,脂代谢对骨质疏松的最终影响也取决于上述多因素的相对平衡。

综上所述:绝经后 2 型糖尿病患者的 HDL-C 与骨吸收指标呈明显正相关关系,HDLC 增高可能加快骨转换,降低骨密度,从而容易发生骨质疏松。临床中对于脂代谢紊乱的患者,降脂治疗、旨在升高高密度脂蛋白的同时注意预防骨质疏松的发生;对于骨质疏松患者,治疗骨质疏松症的同时需要联合调

脂的综合治疗。

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密度的风险,本研究通过对女性骨密度的 Logistic 回归分析发现,饮酒为 OP 的保护因素( $B = 0.243, P = 0.000$ ),饮酒与 OP 关系不一致可能与女性适量饮酒有关,因此我们推断,适量饮酒可以降低发生 OP 的风险,至于是否还有其他原因值得我们后期的研究探讨。同时研究表明:体重、身高和 BMI 与 OP 的关系不一致,可能与不同种族和个体的遗传因素有关。通过对 BMI 与无骨质增生女性 OP 的 Logistic 回归分析,为证实 BMI 是否为 OP 的保护因素,为 OP 的防治提供了一定依据。

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## 绝经后2型糖尿病患者血脂与骨代谢的关系

作者: 征海华, 雷涛, 江东梅, 戚蓓蓓, 宋文春  
作者单位: 征海华, 江东梅, 戚蓓蓓, 宋文春(东南大学附属盐城医院内分泌科, 盐城, 224001), 雷涛(同济大学附属同济医院内分泌科)  
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