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## 2型糖尿病骨密度与冠状动脉钙化积分相关性研究\*

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**摘要 目的:**探讨2型糖尿病患者冠脉钙化积分与骨密度的关系。**方法:**入选在2015年6月至2017年6月我科住院的2型糖尿病患者98例,按照性别以及糖化血红蛋白8%、低密度脂蛋白2.6 mmol/L、身高体重指数<24 kg/m<sup>2</sup>为切点分为两组,进行冠脉动脉CT检查,计算冠脉动脉总钙化积分,依照钙化积分等于0为阴性组,大于0为阳性组。同时检测患者的骨密度、骨代谢指标、血钙、血磷等水平。比较冠脉钙化积分和骨代谢指标及骨密度的相关性。**结果:**1)男性患者中:阳性组糖化血红蛋白和颈部血管斑块形成明显高于阴性组,差异有统计学意义。女性患者中:阳性组年龄、颈部血管内膜厚度、高血压病史明显高于阴性组,差异有统计学意义。2)阳性、阴性两组之间骨代谢指标差异无统计学意义。3)男性患者中:阳性组腰椎骨密度明显高于阴性组,差异有统计学意义。女性患者中阳性组的腰椎骨密度明显低于阴性组,差异有统计学意义,在控制混杂因素以后,两组间差异无统计学意义。4)分别在男性和女性患者中按照年龄为60岁分为两组,两组间阳性组与阴性组的骨代谢指标及骨密度差异无统计学意义。**结论:**在2型糖尿病患者中,冠脉钙化积分和骨代谢以及骨密度之间无明显相关性。

**关键词:**2型糖尿病;骨密度;骨代谢指标;冠脉钙化积分

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## The Relationship between Bone Mineral Density and Coronary Artery Calcification Score in Type 2 Diabetic Patients\*

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**ABSTRACT Objective:** To investigate the relationship between coronary artery calcification score and bone mineral density in type 2 diabetic patients. **Methods:** 98 type 2 diabetes patients hospitalized in our department from June 2015 to June 2017 were measured BMD, coronary artery calcification score, bone metabolic markers, calcium and phosphorus. And patients were divided into two groups according to sex, HbA1c, LDL and BMI. The correlation between coronary calcification score and bone metabolic markers bone mineral density was compared. **Results:** 1) Among the male patients, the HbA1c and Cervical vascular plaque of the positive group was significantly higher than the negative group. Among the female patients, the age, cervical vessel intimal thickness and history of hypertension of the positive group were significantly higher than the negative group. 2) there was no significant difference in bone metabolic markers between the two groups. 3) Among male patients: lumbar spine BMD of the positive group was significantly higher than the negative group. Among the female patients, the lumbar spine BMD of the positive group was significantly lower than the negative group. After controlling the confounding factors, there was no statistical difference between the two groups. 4) Divided into two groups according to age, there was no significant difference in bone metabolic markers and BMD. **Conclusions:** There is no significant correlation between coronary artery calcification score and bone metabolic markers, BMD in type 2 diabetes patients.

**Key words:** Type 2 diabetes; Bone mineral density; Bone metabolic markers; Coronary artery calcification score

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### 前言

随着我国社会人口老龄化的日益严重,糖尿病、骨质疏松症和动脉粥样硬化症已成为老年人常见病、多发病,且有年轻化趋势。而糖尿病是骨质疏松症和动脉硬化症的共同危险因

素<sup>[1,2]</sup>。有学者认为骨质疏松症与动脉硬化之间没有内在联系,也有学者认为这两种疾病有一定的相关性和共同发病机理<sup>[3-5]</sup>。冠脉CT血管成像是确诊冠心病的金标准,钙化积分(CACS)是评估冠脉粥样硬化存在与否及严重程度的可靠指标<sup>[6]</sup>。本文拟探讨在2型糖尿病患者中冠脉钙化和骨代谢以及骨密度之

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间的关系,为冠状动脉粥样硬化与骨质疏松防治提供依据。

## 1 资料与方法

### 1.1 一般资料

观察 2015 年 6 月至 2017 年 06 月我院内分泌科住院的 2 型糖尿病患者 1212 例。纳入标准:1)符合 2017 年中国 2 型糖尿病防治指南诊断标准;2) 病程  $\geq 5$  年;3) 血压  $\leq 180/110$  mmHg;4) 体重指数  $\leq 35 \text{ kg/m}^2$ ;5) 知情同意,自愿受试。排除标准:糖尿病危急重症、严重肝肾功能不全、恶性肿瘤、合并血液系统疾病及其他代谢性疾病等。按照纳入及排除标准,入选 126 人进行冠脉 CTA 检查,其中有 28 人因心率超过 75 次/分、屏气时间少于 10 秒、心律不齐及早搏等因素造成未能完成冠脉 CTA 或者冠脉 CTA 图像不清晰而被剔除。最终入选 98 人作为研究对象。其中男性 52 人(年龄 39~75 岁),女性 46 人(均为绝经后女性)。

### 1.2 研究方法

所有患者入院时询问其病程、高血压病史、烟酒史,测量身高,体重,腰围。测血糖、糖化血红蛋白、血脂、骨代谢指标、甲状旁腺激素、同型半胱氨酸、血钙、血磷、颈部血管超声。

**1.2.1 冠脉钙化积分检测** 轴向横截面进行双源 CT 检查,DSCT 平扫病变密度  $>130\text{HU}$  为钙化,分别计算右冠状动脉、左冠状动脉主干、左前降支、回旋支的 TCS 及钙化积分,钙化积分为斑块 CT 面积与峰值系数的乘积。

**1.2.2 骨密度检测** 应用美国 GE 公司的 Lunar iDXA 的双能 X 线骨密度仪,测量患者腰椎、股骨颈和全髋的骨密度值(BMD: $\text{g/cm}^2$ )。

### 1.3 分组

入选 98 例患者中,男性 52 人(年龄 39~75 岁,其中  $<60$  岁 30 人,  $\geq 60$  岁 21 人),女性为 46 人(均为绝经后女性,其中  $<60$  岁 16 人,  $\geq 60$  岁 31 人),进行冠脉动脉双源 CT 检查,计算冠脉动脉总钙化积分,依照钙化积分等于 0 为阴性组,大于 0 为阳性组。同时检测患者的骨密度、骨代谢指标、血钙、血磷等水平。比较冠脉钙化积分和骨代谢指标及骨密度的相关性。分别对男性和女性患者按照年龄为 60 岁分为两组,比较不同年龄层内冠脉钙化积分与骨密度的相关性。

### 1.4 统计学方法

应用 SPSS19.0 统计软件进行统计学分析。分析正态分布资料以  $\bar{x} \pm s$  表示,组间比较采用 t 检验。计数资料用频数和  $\chi^2$  检验。使用协方差分析控制混杂因素。 $P < 0.05$  视为差异有统计学意义。

## 2 结果

### 2.1 男性患者

**2.1.1 一般资料比较** 阳性组糖化血红蛋白(HbA1c)( $P=0.044$ )和颈部血管斑块形成( $P=0.006$ )明显高于阴性组,差异有统计学意义(表 1),两组间骨代谢指标无差异。

表 1 男性患者中冠脉钙化积分阴性组和阳性组一般资料的比较

Table 1 The comparison of general data between the negative and positive group according to coronary artery calcification score in male patients

Factors	Negative Group (n=31)	Positive group (n=21)
Age	$55.64 \pm 9.99$	$58.23 \pm 9.54$
Height (cm)	$167.39 \pm 7.55$	$170.90 \pm 5.88$
Weight (kg)	$72.00 \pm 12.417$	$76.17 \pm 9.793$
BMI ( $\text{kg}/\text{cm}^2$ )	$25.26 \pm 4.044$	$26.22 \pm 3.503$
Waist circumference (cm)	$90.10 \pm 8.219$	$91.24 \pm 10.511$
Illness duration (year)	$10.03 \pm 3.507$	$11.14 \pm 4.725$
Hypertension	17/31	16/21
History of smoking and drinking	23/31	18/21
HbA1c (%)	$7.981 \pm 1.801$	$9.195 \pm 2.446^a$
Blood pressure (mmol/L)	$8.30 \pm 2.740$	$9.968 \pm 4.687$
LDL-C (mmol/L)	$2.793 \pm 2.126$	$2.763 \pm 0.815$
Blood calcium (mmol/L)	$2.249 \pm 0.147$	$2.288 \pm 0.152$
Blood phosphorus (mmol/L)	$1.241 \pm 0.162$	$1.196 \pm 0.210$
PTH (mmol/L)	$4.606 \pm 1.680$	$4.224 \pm 1.913$
HCY(umol/L)	$15.27 \pm 5.716$	$17.167 \pm 4.503$
Neck intima thickness (cm)	$0.634 \pm 0.132$	$0.702 \pm 0.160$
Neck vascular plaque formation	8/31	15/21 <sup>a</sup>

Note: a The comparison of coronary artery calcification score between negative and positive group,  $P < 0.05$ .

**2.1.2 骨代谢指标及骨密度** 两组间骨代谢指标:25-羟维生素 D(25-OH-VD)、总 I 型前胶原氨基端延长肽(TP1NP)、 $\beta$ -胶原降解产物( $\beta$ -CTX)、骨钙素差异无统计学意义(表 2)。阳性组腰椎 BMD 明显高于阴性组( $P < 0.05$ ),差异有统计学意义,股骨

颈和全髋 BMD 的差异无统计学意义。在控制 HbA1c 和颈部血管斑块形成后,阳性组的腰椎 BMD 仍明显高于阴性组,差异有统计学意义( $P < 0.05$ )(表 2)。

表 2 男性患者中冠脉钙化积分阴性组和阳性组骨代谢指标及骨密度的比较

Table 2 The comparison of bone metabolic markers, bone mineral density between the negative and positive group according to coronary artery calcification score in male patients

Factors	Negative Group (n=31)	Positive group (n=21)
25-OH-VD (ug/L)	20.45± 8.354	17.62± 7.652
Osteocalcin (ug/L)	13.13± 6.084	13.71± 6.951
β-CTX (ug/L)	0.503± 0.159	0.310± 0.205
TP1NP (ug/L)	31.23± 16.068	35.48± 18.140
BMD (Lumbar vertebra) (g/cm <sup>2</sup> )	1.149± 0.139	1.290± 0.198 <sup>a</sup>
BMD (Femoral neck) (g/cm <sup>2</sup> )	0.956± 0.134	0.988± 0.160
BMD (Hip) (g/cm <sup>2</sup> )	1.039± 0.135	1.057± 0.160

Note: a The comparison of coronary artery calcification score between negative and positive group,  $P<0.05$ .

2.1.3 按照年龄为 60 岁分为两组, 比较不同年龄层下冠脉钙化积分与骨密度之间的相关性 按照年龄为 60 岁分为两组, 无论是在年龄<60 岁还是≥ 60 岁的男性患者中, 冠脉钙化阴性组与阳性组之间骨代谢指标及骨密度无明显相关性。

表 3 比较不同年龄水平下男性患者冠脉钙化积分和骨代谢以及骨密度之间的关系

Table 3 The relationship between coronary artery calcification score and bone metabolic markers, bone mineral density under different age levels in male patients

Groups	Age<60 year old (n=30)		Age≥ 60 year old (n=21)	
	Negative group (n=19)	Positive group(n=11)	Negative group (n=11)	Positive group (n=10)
25-OH-VD (ug/L)	20.947± 9.454	17.818± 6.646	19.818± 6.853	17.400± 8.997
Osteocalcin (ug/L)	14.684± 7.016	13.546± 6.904	9.818± 3.945	13.900± 7.370
β-CTX (ug/L)	0.311± 0.152	0.309± 0.197	0.864± 1.940	0.310± 0.223
TP1NP (ug/L)	30.632± 15.439	36.909± 22.407	33.182± 18.170	33.900± 12.965
BMD (Lumbar vertebra) (g/cm <sup>2</sup> )	1.146± 0.146	1.275± 0.169	1.140± 0.128	1.307± 0.234
BMD (Femoral neck) (g/cm <sup>2</sup> )	0.955± 0.132	1.000± 0.144	0.931± 0.117	0.974± 0.182
BMD (Hip) (g/cm <sup>2</sup> )	1.037± 0.141	1.066± 0.162	1.020± 0.112	1.047± 0.166

## 2.2 女性患者

压病史明显高于阴性组, 差异有统计学意义(表 4)。

2.2.1 一般资料比较 阳性组年龄、颈部血管内膜厚度、高血

表 4 女性患者中冠脉钙化积分阴性组和阳性组一般资料的比较

Table 4 The comparison of general data between the negative and positive group according to coronary artery calcification score in female patients

Factors	Negative group (n=27)	Positive group (n=19)
Age	60.22± 7.797	66.63± 5.993 <sup>a</sup>
Height (cm)	157.78± 6.571	154.37± 4.633
Weight (kg)	61.11± 8.964	61.63± 7.433
BMI (kg/cm <sup>2</sup> )	24.600± 3.212	25.73± 2.454
Waist circumference (cm)	85.48± 7.465	88.74± 6.748
Illness duration (year)	9.85± 3.978	10.53± 4.647
Hypertension	10/27	14/19 <sup>a</sup>
History of smoking and drinking	0/27	0/19
HbA1c (%)	9.00± 2.088	8.453± 1.757
Blood pressure (mmol/L)	7.818± 3.349	9.37± 4.864
LDL-C (mmol/L)	2.662± 0.603	3.192± 1.248
Blood calcium (mmol/L)	2.310± 0.145	2.362± 0.141
Blood phosphorus (mmol/L)	1.349± 1.805	1.334± 0.203
PTH (mmol/L)	4.681± 1.500	4.600± 2.219

HCY(umol/L)	14.337± 3.581	15.242± 4.264
Neck intima thickness (cm)	0.610± 0.167	0.747± 0.120a
Neck vascular plaque formation	13/27	11/19

Note: a The comparison of coronary artery calcification score between negative and positive group,  $P<0.05$ .

**2.2.2 骨代谢指标及骨密度** 两组间骨代谢指标(25-OH-VD、TP1NP、 $\beta$ -CTX、骨钙素)差异无统计学意义。阳性组的腰椎BMD明显低于阴性组( $P<0.05$ ),差异有统计学意义,股骨颈和

全髋BMD的差异无统计学意义。在控制年龄、颈部血管内膜厚度、高血压病史后,阳性组和阴性组的腰椎BMD差异无统计学意义( $P<0.05$ )(表5)。

表5 女性患者中冠脉钙化积分阴性组和阳性组骨代谢指标及骨密度的比较

Table 5 The comparison of bone metabolic markers, bone mineral density between the negative and positive group according to coronary artery calcification score in female patients

Factors	Negative group (n=27)	Positive group (n=19)
25-OH-VD ( $\mu\text{g}/\text{L}$ )	14.15± 5.067	14.63± 6.238
Osteocalcin ( $\mu\text{g}/\text{L}$ )	20.30± 8.637	22.78± 11.466
$\beta$ -CTX ( $\mu\text{g}/\text{L}$ )	0.489± 0.256	0.436± 0.251
TP1NP ( $\mu\text{g}/\text{L}$ )	45.56± 15.164	50.53± 24.318
BMD (Lumbar vertebra) ( $\text{g}/\text{cm}^2$ )	0.967± 0.160	0.881± 0.105 <sup>a</sup>
BMD (Femoral neck) ( $\text{g}/\text{cm}^2$ )	0.807± 0.153	0.781± 0.130
BMD (Hip) ( $\text{g}/\text{cm}^2$ )	0.917± 0.162	0.876± 0.127

Note: a The comparison of coronary artery calcification score between negative and positive group,  $P<0.05$ .

**2.2.3 按照年龄为60岁分为两组,比较不同年龄层下冠脉钙化积分与骨密度的关系** 按照年龄为60岁分为两组,无论是在

年龄<60岁还是≥60岁的女性患者中,冠脉钙化阴性组与阳性组之间骨代谢指标及骨密度无明显相关性。

表6 比较不同年龄水平下女性患者冠脉钙化积分和骨代谢以及骨密度之间的关系

Table 6 The relationship between coronary artery calcification score and bone metabolic markers, bone mineral density under different age levels in female patients

Groups	Age<60 year old (n=16)		Age≥ 60 year old (n=31)	
	Negative group (n=12)	Positive group(n=4)	Negative group (n=16)	Positive group(n=15)
25-OH-VD ( $\mu\text{g}/\text{L}$ )	13.750± 5.276	16.500± 7.767	14.688± 4.963	14.133± 5.986
Osteocalcin ( $\mu\text{g}/\text{L}$ )	20.500± 9.386	21.250± 12.971	19.313± 8.686	21.667± 12.596
$\beta$ -CTX ( $\mu\text{g}/\text{L}$ )	0.525± 0.277	0.525± 0.299	0.444± 0.245	0.412± 0.244
TP1NP ( $\mu\text{g}/\text{L}$ )	45.250± 13.765	58.750± 40.310	44.250± 17.261	48.333± 19.689
BMD (Lumbar vertebra) ( $\text{g}/\text{cm}^2$ )	1.100± 0.158	0.956± 0.093	0.889± 0.117	0.861± 0.101
BMD (Femoral neck) ( $\text{g}/\text{cm}^2$ )	0.933± 0.174	0.922± 0.141	0.740± 0.115	0.743± 0.101
BMD (Hip) ( $\text{g}/\text{cm}^2$ )	1.043± 0.176	0.967± 0.153	0.845± 0.115	0.851± 0.112

### 3 讨论

随着人口老龄化进程的逐渐加快,动脉粥样硬化性疾病和骨质疏松症的发病率显著增加。而糖尿病患者更容易发生骨质疏松和动脉粥样硬化,这可能与胰岛素抵抗与高胰岛素血症有关<sup>[7,8]</sup>。2型糖尿病患者的骨质疏松的发生率可达20~60%<sup>[9]</sup>。而这三者常常发生在同一患者<sup>[10,12]</sup>。

虽然Lee SM等人<sup>[13]</sup>研究发现,腹主动脉钙化积分不仅可能提示严重的冠脉钙化,也是前臂低骨量的一种信号。我国张春华等人<sup>[14]</sup>在糖尿病肾病血液透析患者中的研究也表明冠脉钙化积分和前臂的BMD呈负相关。上述研究均表明血管的钙化与骨量的丢失相平行,骨骼中骨的丢失将会在血管中有“骨”

的形成,即血管的钙化。但在我们的研究结果中,女性患者冠脉钙化积分阴性组和阳性组之间骨密度无明显差异,而在男性患者中,冠脉钙化积分阳性组患者的腰椎骨密度反而较阴性组高。表明无论在男性还是女性患者中,冠脉钙化和骨密度没有明显的相关性。2001年Aoyagi K等人<sup>[15]</sup>对524名中年妇女的研究中发现,如同老年女性一样,骨质疏松和主动脉钙化是两个独立的过程。B.Sinnott等人<sup>[16]</sup>对313名绝经后妇女以及167名男性的调查研究中发现,骨质疏松和冠脉钙化均和年龄呈正相关,但是在校正了年龄因素以后,骨质疏松和冠脉钙化之间的正相关性消失了。Martin L等人<sup>[17]</sup>在弹性纤维假黄瘤患者中研究发现,冠脉和下肢动脉钙化严重的患者的骨密度更低,而这种负相关在调整了年龄以后消失了。

其实基质 GLA 蛋白、骨钙素、I 型胶原和骨形成蛋白等这些参与骨代谢的因子也都参与调节了人动脉粥样硬化的形成。因此, 动脉血管的钙化过程可能是一个积极主动调节的过程, 非常类似于骨矿化<sup>[18]</sup>。伴随着年龄的增长, 骨量的丢失和血管的钙化这两种全身性的改变可能会伴随而行, 而一些混杂因素的参与使得部分研究结果显示骨量丢失和血管钙化相关性。这些混杂因素会导致血管钙化, 同时也对骨的代谢造成了一定的影响, 例如: 钙和矿物质的平衡, 雌激素的缺乏, 老年性的退化过程。多项研究均表明, 老龄化是骨量丢失的主要因素之一<sup>[19-21]</sup>。也有多项研究表示校正了年龄以后, 骨量丢失和血管钙化没有相关性。雌激素的缺乏是一个全身性的因素, 通过加速骨的破坏而导致骨量的丢失<sup>[22-23]</sup>, 通过雌激素受体径路直接作用于动脉壁导致动脉粥样硬化, 这是两个独立的过程。没有证据可以证明活跃的破骨细胞可以参与血管的钙化过程。研究也证明了这一点, 年龄、高血压、糖尿病、锻炼、吸烟为心血管疾病的独立影响因子<sup>[24-27]</sup>, 同样这些也是骨质疏松的危险因素<sup>[6,28-30]</sup>。因此, 低骨密度与血管钙化之间的关系尽管存在共同的危险因素如吸烟、糖尿病、雌激素的缺乏等, 但在调整了其他混杂因素后两者间的关系会消失。本研究在调整了混杂因素以后, 冠脉钙化积分和骨代谢以及骨密度之间无明显相关性。伴随着年龄的增加, 骨质疏松症和动脉粥样硬化疾病是多因素衰老相关的退行性疾病, 是两个独立的进程, 并没有明显的相关性。

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