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中老年2型糖尿病患者骨质疏松性肌少症与血管硬化度的关系研究

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摘　要

目的：探讨2型糖尿病(Type 2 Diabetes Mellitus, T2DM)患者骨质疏松性肌少症与血管硬化度的关系。方法：横断面连续选取215例T2DM住院患者(62.5 ± 7.59岁)，依据臂踝脉搏波传播速度(brachial-ankle Pulse Wave Velocity, baPWV)分为正常A组(<1800 cm/s, n = 112)与高值B组(≥1800 cm/s, n = 103)比较两组一般临床资料及实验室生化指标，分析骨质疏松性肌少症与血管硬化度的关系。结果：1) B组的年龄、糖尿病病程、收缩压(SBP)、收缩压/舒张压(DSP)、高血压史、低肌肉质量指数(skeletal lean mass index, SMI)检出率显著高于A组，肾小球滤过率、六米步速、股骨颈骨量显著低于A组，(P < 0.05)。2) 在T2DM患者、收缩压 < 140 mmHg T2DM患者、年龄 < 75岁患者中，单纯肌少症组、骨质疏松性肌少症组的baPWV异常检出率均高于正常组，差异有统计学意义，P < 0.05；单纯骨质疏松组与正常组、单纯肌少症组、骨质疏松性肌少症组的baPWV检出率均无统计学差异，肌少症组与骨质疏松性肌少症组的baPWV检出率均无统计学差异。3) Logistic回归分析显示，T2DM病程大于10年、年龄大于等于75岁，SBP大于等于140 mmHg和骨质疏松合并肌少症增加了baPWV异常的发生危险，差异有统计学意义，(0R = 2.080, 95% CI: 1.122~3.853, P = 0.020, 0R = 15.704, 95% CI: 1.664~148.183, P = 0.016, 0R = 2.976, 95% CI: 1.534~5.772, p = 0.001, 0R = 10.359, 95% CI: 1.941~55.270, P = 0.006)。结论：在中老年T2DM患者中，长病程、高龄、不达标的SBP和骨质疏松性肌少症是baPWV异常的危险因素，且在血压正常人群中骨质疏松性肌少症仍与baPWV异常关系密切。

关键词

糖尿病，2型，肌少症，骨质疏松症，骨质疏松性肌少症，臂踝脉搏波传播速度

Relationship between Osteosarcopenia and the Degree of Vascular Sclerosis in Middle-Aged and Elderly Patients with Type 2 Diabetes Mellitus

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Abstract

Objective: To investigate the relationship between osteosarcopenia and vascular sclerosis in Type 2 Diabetes Mellitus (T2DM) patients. Methods: 215 hospitalized T2DM patients (62.5 ± 7.59 years old) were continuously selected and divided into normal group A (<1800 cm/s, n = 112) and high value group B (≥1800 cm/s, n = 103) were compared with the general clinical data and laboratory biochemical indexes of the two groups, and the relationship between osteosarcopenia and vascular sclerosis was analyzed. Results: 1) Age, diabetes course, systolic blood pressure (SBP), systolic/diastolic blood pressure (DSP), history of hypertension, and low muscle mass index (SMI) of group B were significantly higher than those of group A, while glomerular filtration rate, 6-meter stride speed and femoral neck bone mass were significantly lower than those of group A (P < 0.05). 2) Among T2DM patients, systolic blood pressure < 140 mmHg T2DM patients and patients aged < 75 years, the abnormal detection rate of baPWV in simple sarcosis group and osteoporotic sarcosis group was higher than that in normal group, with statistical significance (P < 0.05); there was no statistical difference in baPWV detection rate between pure osteoporosis group and normal group, simple sarcopenia group and osteoporotic sarcopenia group. There was no statistical difference in baPWV detection rate between sarcopenia group and osteoporotic sarcopenia group. 3) Logistic regression analysis showed that the disease course of T2DM was greater than 10 years, the age was greater than or equal to 75 years, SBP was greater than or equal to 140 mmHg, osteoporosis combined with sarcosis increased the risk of baPWV abnormality, and the difference was statistically significant (0R = 2.080, 95% CI: 1.122~3.853, P = 0.020, 0R = 15.704, 95% CI: 1.664~148.183, P = 0.016, 0R = 2.976, 95% CI: 1.534~5.772, P = 0.001, 0R = 10.359, 95% CI: 1.941~55.270, P = 0.006). Conclusion: In middle-aged and elderly T2DM patients, long disease course, old age, sub-standard SBP and osteoporotic sarcopenia are risk factors for baPWV abnormality, and osteoporotic sarcopenia is still closely related to baPWV abnormality in normal blood pressure population.

Keywords

Diabetes Mellitus, Type 2, Sarcopenia, Osteosarcopenia, baPWV

1. 引言

随着生活水平的提高和老龄化社会的推进，我国 T2DM 的患病率已达 11.2% [1]。心血管疾病(CVD)是 T2DM 患者发病率和死亡率的主要原因[2]。动脉粥样硬化是 T2DM 常见的血管并发症[3]，与许多心脑血管疾病密切相关，常发生在明显的糖尿病微血管和大血管并发症之前[4]。baPWV 是评估血管硬化度的良好指标，目前都是采用 1400 cm/s 为评价脉搏波传导速度异常的临界值[5]，2 型糖尿病患者会更早的

发生动脉硬化，甚至在糖尿病前期血管顺应性就已出现改变，所以 baPWV 测得的值普遍大于正常参考值(1400 cm/s)，有文献指出，baPWV ≥ 1800 cm/s 对心血管事件发生有预测价值[6]。在中老年 T2DM 患者中肌少症[7]、骨质疏松症患病率明显增高[8]。研究证实骨骼肌质量减少[8]或功能下降[9]与动脉硬化密切相关，但骨密度与血管硬化的关系不明确[10]。近年来骨质疏松性肌少症(Osteosarcopenia)作为一个新概念被提出[11]，即骨质疏松症和肌少症同时存在的综合征[12]，其在中老年 T2DM 患者中与血管硬化度的关系目前尚不明确。因此，本研究以 baPWV 1800 cm/s 为切点，旨在探讨中老年 T2DM 患者骨质疏松性肌少症与血管硬化度的关系，为 T2DM 合并骨质疏松性肌少症人群及早关注动脉硬化提供临床依据。

2. 资料与方法

2.1. 研究对象

选取在秦皇岛市第一医院内分泌科住院的 T2DM 患者，纳入标准：1) 年龄 50 岁以上(女性已绝经)；2) 具备基本沟通、理解能力和完全行为能力。排除标准：1) 未纠正的糖尿病急性并发症如糖尿病酮症酸中毒、高渗性高血糖状态；2) 急性脑血管病、急慢性肝、肾功能衰竭等伴有严重身体损害病史的患者；3) 患有影响日常活动的严重骨关节病或神经肌肉疾病患者；4) 急性感染性疾病患者；5) 恶性肿瘤患者。符合纳入标准的患者均签署秦皇岛市第一医院伦理委员会(2020B004)批准的知情同意书，共有 215 例 T2DM 患者纳入，年龄(62.5 ± 7.59 岁)，男性 100 例，女性 115 例。

2.2. 诊断标准

2.2.1. 骨质疏松症

以腰椎、股骨颈的 T 值 ≤ −2.5 为骨质疏松诊断切点[13]。单纯骨质疏松组为在非肌少症人群诊断为骨质疏松患者。

2.2.2. 肌少症诊断标准

肌少症：SMI 低于参考值(男性 SMI < 7.0 kg/m^2，女性 SMI < 5.4 kg/m^2)，且男性握力 < 28 kg，女性握力 < 18 kg (和)或步行 6 米速度 < 1.0 米/秒[14]；单纯肌少症组为在非骨质疏松人群诊断为肌少症患者。

2.2.3. 骨质疏松性肌少症诊断标准

具备肌少症合并骨质疏松[11]。

2.3. 方法

2.3.1. 调查内容

1) 记录患者的性别、年龄、糖尿病病程、高血压史、吸烟饮酒史、脆性骨折史。

2) 人体指标测量：记录入组时 SBP、DBP、身高、体重、计算体质量指数(Body Mass Index, BMI)、腰围(Waist Circumference, WC)、6 米步速、JAMAR 电子握力计测量握力(左右手分别握两次，取最大值)、应用法国 MEDILINK 骨密度仪器测量骨矿含量(Bone Mineral Content, BMC)、腰椎 L1-4 (Bone Mineral Density, BMD)、股骨颈 BMD、全身肌肉含量、计算四肢 SMI。

3) 血标本检测：空腹收集静脉血清，日立 LST008 全自动生化仪检测空腹血糖(Fasting Blood-Glucose, FBG)、糖化血红蛋白(HbA1c)、甘油三酯(Triglyceride, TG)、胆固醇(Cholesterol, CHO)、高、低密度脂蛋白胆固醇(High Density Lipoprotein Cholesterol, HDL-C, Low Density Lipoprotein Cholesterin, LDL-C)、血尿酸(Uric Acid, UA)、血(Credtinine, Cr)、并计算估算肾小球滤过率(estimated Glomerular Filtration Rate, eGFR)。

2.3.2. 分组

依据 baPWV 在血管硬化度中的预测价值，以 1800 cm/s 为切点值，baPWV < 1800 cm/s 为正常组(A 组)；baPWV ≥ 1800 cm/s 为高值组(B 组) [5]。

2.3.3. 统计

采用 SPSS 26.0 软件对数据进行分析，计量资料以均数 ± 标准差表示，计数资料用例数百分数表示。组间变量比较采用独立样本 t 检验，计数资料比较采用趋势 χ^2 检验，多因素风险分析采用 Logistic 回归分析。以 $P < 0.05$ 为差异有统计学意义。

3. 结果

3.1. A、B 两组组间基线资料比较

研究人群单纯肌少症检出率为 23.3%，单纯骨质疏松占 17.2%，骨质疏松症合并肌少症达 5.1%，baPWV 异常检出率为 47.9%。B 组的年龄、糖尿病病程、SBP、SBP/DBP、高血压史、低 SMI 检出率显著高于 A 组，B 组 eGFR、六米步速、股骨颈 BMD 显著低于 A 组，差异具有统计学意义($P < 0.05$)。两组间在性别、BMI、WC、HbA1c、FBP、HDL-C、LDL-C、UA、SMI、握力、腰椎 L1-4 BMD 无统计学差异($P > 0.05$)，见表 1。

3.1.1. 在糖尿病患者中，骨质疏松性肌少症各组间 baPWV 异常检出率比较

单纯肌少症组(62.0%)、骨质疏松性肌少症组(81.8%)的 baPWV 异常检出率高于正常组(35.0%)，差异有统计学意义，$P < 0.05$；单纯骨质疏松组与正常组、单纯肌少症组、骨质疏松性肌少症组的 baPWV 检出率均无统计学差异，肌少症组与骨质疏松性肌少症组的 baPWV 检出率无统计学差异，见表 2。

3.1.2. 在收缩压小于 140 mmHg 糖尿病患者中，骨质疏松性肌少症各组间 baPWV 异常检出率比较

单纯肌少症组(50.0%)、骨质疏松性肌少症组(100%)的 baPWV 异常检出率高于正常组(18.2%)，差异有统计学意义，$P < 0.05$；单纯骨质疏松组与正常组、单纯肌少症组、骨质疏松性肌少症组的 baPWV 检出率均无统计学差异，肌少症组与骨质疏松性肌少症组的 baPWV 检出率无统计学差异，见表 3。

3.1.3. 在年龄小于 75 岁糖尿病患者中，骨质疏松性肌少症各组间 baPWV 异常检出率比较

单纯肌少症组(60.4%)、骨质疏松性肌少症组(81.8%)的 baPWV 异常检出率高于正常组(34.5%)，差异有统计学意义，$P < 0.05$；单纯骨质疏松组与正常组、单纯肌少症组、骨质疏松性肌少症组的 baPWV 检出率均无统计学差异，肌少症组与骨质疏松性肌少症组的 baPWV 检出率无统计学差异，见表 4。

3.2. baPWV 的 Logistic 回归分析

以 baPWV 为因变量(赋值 0 = A 组，1 = B 组)，以糖尿病病程(0 = <10 年，1 = ≥10 年)，年龄(0 = <75 岁，1 = ≥75 岁)，eGFR (0 = ≥90 mL/min, 1 = <90 mL/min)，口服降压药，(0 = 未服药，1 = 正在服药)，SBP (0 = <140 mmHg, 1 = ≥140 mmHg)，骨质疏松性肌少症(0 = 正常组，1 = 单纯肌少组，2 = 单纯骨松组，3 = 骨质疏松合并肌少症组)为自变量，行二元 Logistic 回归分析显示，T2DM 病程大于 10 年、年龄大于等于 75，SBP 大于等于 140 mmHg 和骨质疏松合并肌少症增加了 baPWV 异常的发生危险，差异有统计学意义，(0R = 2.080, 95% CI: 1.122~3.853, P = 0.020, 0R = 15.704, 95% CI: 1.664~148.183, P = 0.016, 0R = 2.976, 95% CI: 1.534~5.772, P = 0.001, 0R = 10.359, 95% CI: 1.941~55.270, P = 0.006)，见表 5。

Table 1. Comparison of baseline data between groups A and B
表 1. A、B 两组间基线资料比较

变量	A (n = 112)	B (n = 103)	t 值/x^2	P
男性(n, %)	49 (43.8%)	51 (49.5%)	0.717	0.397
年龄(岁)	59.88 ± 7.084	65.36 ± 7.099	−5.665	0.000
T2DM 病程(年)	7.134 ± 6.545	12.08 ± 8.723	−4.719	0.000
吸烟(n, %)	30 (26.8%)	19 (18.4%)	2.120	0.145
饮酒(n, %)	26 (23.2%)	19 (18.4%)	0.737	0.391
高血压(n, %)	64 (57.1%)	76 (73.8%)	6.543	0.011
血脂异常(n, %)	99 (88.4%)	92 (89.3%)	0.047	0.829
低 SMI (n, %)	56 (45.0%)	67 (55.0%)	4.964	0.026
慢步速(n, %)	43 (38.4%)	51 (49.5%)	2.697	0.101
低握力(n, %)	24 (21.4%)	30 (29.1%)	1.690	0.194
单纯肌少症(n, %)	19 (17.0%)	31 (30.1%)	18.785	0.000
单纯骨质疏松(n, %)	15 (13.4%)	22 (21.4%)	18.785	0.000
骨质疏松性肌少症(n, %)	2 (1.8%)	9 (5.1%)	18.785	0.000
SBP (mmHg)	138.67 ± 19.013	147.67 ± 19.587	−3.418	0.001
DBP (mmHg)	83.76 ± 11.404	86.12 ± 10.921	−1.545	0.124
SBP/DBP	1.67 ± 0.204	1.73 ± 0.232	−2.043	0.042
BMI (kg/cm^2)	25.66 ± 3.343	25.33 ± 3.220	0.738	0.461
WC (cm)	91.136 ± 8.895	92.57 ± 9.910	−1.141	0.255
FBG (mmol/L)	8.88 ± 3.470	8.90 ± 3.412	−0.038	0.970
HbA1c (%)	9.04 ± 2.221	8.79 ± 1.834	0.879	0.381
eGFR (ml/min)	101.00 ± 15.916	93.81 ± 18.568	3.056	0.003
UA (umol/L)	300.01 ± 105.421	317.96 ± 96.533	0.872	0.384
TG (mmol/L)	2.06 ± 1.482	2.20 ± 1.626	−0.643	0.521
TC (mmol/L)	5.33 ± 1.594	5.37 ± 1.520	−0.211	0.833
HDL-C (mmol/L)	1.04 ± 0.266	1.03 ± 0.226	0.183	0.855
LDL-C (mmol/L)	2.90 ± 0.967	2.89 ± 1.055	0.096	0.924
SMI (kg/m^2)	6.04 ± 0.917	5.86 ± 0.846	1.525	0.129
握力(kg)	27.50 ± 9.716	25.78 ± 9.151	1.332	0.184
六米步速(m/s)	1.06 ± 0.189	0.99 ± 0.211	2.400	0.017
BMD L1-4 (g/cm^2)	0.92 ± 0.146	0.90 ± 0.179	0.747	0.456
BMD neck (g/cm^2)	0.81 ± 0.113	0.77 ± 0.143	2.703	0.007

注：baPWV < 1800 为 A 组；baPWV ≥ 1800 为 B 组。

Table 2. Comparison of abnormal detection rate of baPWV among osteosarcopenia groups
表 2. 骨质疏松性肌少症各组间 baPWV 异常检出率比较

分组	合计(例)	A (n = 112)	B (n = 103)	X^2	P
正常组(n, %)	117	76 (65.0%)	41 (35.0%)	18.79	0.000
单纯肌少症(n, %)	50	19 (38.0%)	31* (62.0%)		
单纯骨质疏松(n, %)	37	15 (40.5%)	22 (59.5%)		
骨质疏松性肌少症(n, %)	11	2 (18.2%)	9* (81.8%)		

注：*与正常组相比，具有统计学差异。

Table 3. Comparison of abnormal detection rate of baPWV in patients with osteoporotic sardonia with systolic blood pressure < 140 mmHg
表 3. 收缩压 < 140 mmHg 人群，骨质疏松性肌少症各组间 baPWV 异常检出率比较

分组	合计 (例)	A (n = 54)	B (n = 30)	X^2	P
正常组(n, %)	44	36 (81.8%)	8 (18.2%)	18.60	0.000
单纯肌少症(n, %)	22	11 (50.0%)	11* (50.0%)		
单纯骨质疏松(n, %)	12	7 (58.3%)	5 (41.7%)		
骨质疏松性肌少症(n, %)	6	0 (0.00%)	6* (100%)		

注：*与正常组相比，具有统计学差异。

Table 4. Comparison of abnormal detection rate of baPWV in osteoporotic sarcopenia among groups aged less than 75 years
表 4. 年龄小于 75 岁人群，骨质疏松性肌少症各组间 baPWV 异常检出率比较

分组	合计(例)	A (n = 110)	B (n = 93)	X^2	P
正常组(n, %)	113	74 (65.5%)	39 (34.5%)	16.10	0.001
单纯肌少症(n, %)	48	19 (39.6%)	29* (60.4%)		
单纯骨质疏松(n, %)	31	15 (48.4%)	16 (51.6%)		
骨质疏松性肌少症(n, %)	11	2 (18.2%)	9* (81.8%)		

注：*与正常组相比，具有统计学差异。

Table 5. Binary Logistic regression analysis between different baPWV groups
表 5. 不同 baPWV 组间的二元 Logistic 回归分析

	B	*OR*	*95% CI*	P
病程	0.732	2.080	1.122~3.853	0.020
年龄	2.754	15.704	1.664~148.183	0.016
eGFR	0.506	1.658	0.782~3.516	0.187
SBP	1.090	2.976	1.534~5.772	0.001
口服降压药	0.184	1.202	0.641~2.254	0.566
正常组	--	--	Ref	0.001
单纯肌少组	1.269	3.557	1.673~7.561	0.001
单纯骨松组	0.912	2.490	1.071~5.790	0.034
骨质疏松性肌少组	2.338	10.359	1.941~55.270	0.006
常量	−1.976	0.139	--	0.000

4. 讨论

我国逐渐步入老龄化社会，T2DM 和肌少症、骨质疏松都是与增龄相关的常见慢性疾病[15]。骨质疏松性肌少症是一种独特的综合征[16]，由骨质疏松和低肌肉质量、力量和/或功能(肌肉减少症)的结合定义。人口老龄化的加速，骨质疏松性肌少症发病率将不可避免地增加，导致更多的跌倒、骨折和住院[17] [18]。动脉硬化，是一种导致血管弹性减低、血管壁钙化和血流限制现象[19]。动脉硬化与糖尿病之间的关系是双向的[20]，有文献报道，糖尿病或血糖升高将会损伤血管壁，导致动脉硬化加速，同时随着 baPWV 升高，糖尿病的发生风险也逐渐增高[21]，一项开滦研究显示，与非动脉硬化组相比，动脉硬化组糖尿病风险的 HR (95% CI)分别为 2.11 (1.71, 2.61) [22]。脉搏波速度(PWV)测量被公认是最简单、无创、可靠、重复性好的动脉僵硬度测定方法[23]，适用于大规模人群流行病学研究[24]。在一些社区居住的老年人和冠心病患者的队列中，baPWV 是心血管事件和死亡的独立预测因子[25]。

动脉硬化与肌少症之间有着交互关系。肌少症的潜在发病机制包括低体力活动、氧化应激和胰岛素抵抗的增加、与衰老相关激素的变化和炎症因子水平的增加，这些已被证明可促进动脉硬化的发生[9]。动脉硬化会导致血液、氧气和营养物质向肌肉组织的流动减少，从而导致肌肉质量的损失[26]。动脉硬化与骨质疏松之间也有着密切关系，这是由于骨和血管细胞有共同的成骨和矿化过程[27]。两种慢性疾病的平行进展，导致心血管事件增加，骨折风险上升[28]。本研究 T2DM 患者骨质疏松性肌少症检出率占 5.1%，A、B 两组间的六米步速、低 SMI 检出率和股骨颈骨量存在差异，这提示我们 T2DM 患者的肌肉功能、质量和骨量与 baPWV 有一定关系，在 Logistic 回归中进一步证实了 T2DM 中老年人群骨质疏松性肌少症是 baPWV 异常的危险因素。我们还发现，中老年 T2DM 患者长病程、高龄、收缩压增高也是是血管硬化的风险因素。在对血压的分层研究，我们发现收缩压正常糖尿病患者中单纯肌少症组、骨质疏松性肌少症组的baPWV异常检出率显著高于正常组；且在小于75岁的年龄分层中我们同样发现单纯肌少症组、骨质疏松性肌少症组的 baPWV 异常检出率显著高于正常组，而单纯骨质疏松组的 B 组检出率与正常组无统计学差异。这一结果提示我们在中老年 2 型糖尿病患者中校正血压、年龄因素后，肌少症、骨质疏松性肌少症与血管硬化度关系依然密切，单纯骨质疏松与血管硬化度关系不明显。

本研究也有一定的局限性。首先，由于这是一项横断面研究，不利于确定因果关系。其次，本研究的样本量相对较小且为单中心研究，研究结果有待多中心验证。

总之，我们研究明确了在中老年 T2DM 患者中，长病程、高龄、不达标的 SBP 和骨质疏松性肌少症状态是 baPWV 异常的危险因素。因此在发生骨质疏松性肌少症时要重视血管硬化的管理。在强调糖尿病患者综合管理的同时，也要增加抗阻运动，从而有益于血管的维护，有望降低心脑血管不良事件的发生。

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