

· 论 著 ·

不同中医证型 2 型糖尿病患者血糖波动指标与骨骼肌含量的关系

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摘要: 目的 探究 2 型糖尿病(T2DM)不同中医证型患者血糖波动指标与骨骼肌含量的差异及相关性。方法 采用回顾性研究的方法,选取 2020 年 9 月至 2021 年 9 月在上海中医药大学附属曙光医院内分泌科住院的 T2DM 患者 330 例,根据中医证型不同分为气阴两虚证($n=169$)、阴虚燥热证($n=88$)、湿热困脾证($n=73$)。观察不同证型间血糖波动相关指标[目标范围内时间(TIR)、血糖标准差(SDBG)、24 h 平均血糖波动幅度(MAGE)、日间血糖平均绝对差(MODD)、血糖变异系数(CV)、糖化血红蛋白(HbA1c)]的差异,骨骼肌含量相关指标[相对骨骼肌质量指数(RASM)、四肢骨骼肌质量(ASM)、全身总肌肉质量(TLM)]的差异,分析不同证型 T2DM 患者中两者之间的相关性。以 TIR $\geq 70\%$ 为达标。结果 气阴两虚证组 TIR 达标率为 46.7%,阴虚燥热证组为 30.7%,湿热困脾证组为 47.9%,三组 TIR 达标率比较差异有统计学意义($\chi^2=7.145, P=0.028$),且气阴两虚证组和湿热困脾证组的 TIR 达标率明显高于阴虚燥热组($P<0.05$)。湿热困脾证组 SDBG、MAGE、MODD、CV 均低于气阴两虚证组及阴虚燥热证组($P<0.05$),气阴两虚证组 ASM 低于阴虚燥热证组及湿热困脾证组($P<0.05$),差异均有统计学意义。阴虚燥热证组中,RASM 分别与 SDBG($r=-0.234, P=0.029$)、MODD($r=-0.248, P=0.029$)、CV($r=-0.355, P=0.001$)呈显著负相关。**结论** T2DM 不同证型间血糖波动及骨骼肌含量存在差异,阴虚燥热证血糖波动与骨骼肌含量存在相关性。

关键词: 2 型糖尿病; 中医证型; 血糖波动; 骨骼肌质量; 气阴两虚证; 阴虚燥热证; 湿热困脾证

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Relationship between blood glucose fluctuation and skeletal muscle in type 2 diabetes mellitus patients with different Chinese medicine syndrome types

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Abstract: Objective To explore the associations of blood glucose fluctuation indexes with skeletal muscle content in different Chinese medicine syndromes of type 2 diabetes mellitus (T2DM). **Methods** A retrospective study was performed on 330 T2DM patients hospitalized in Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine from September 2020 to September 2021. According to different Chinese medicine syndrome, the patients were divided into Qi and Yin deficiency syndrome ($n=169$), dryness-heat due to Yin deficiency syndrome ($n=88$) and damp-heat tapping spleen syndrome ($n=73$). For analyzing the relationship between blood glucose fluctuation and skeletal muscle content, the following indicators were observed and compared among the patients with different syndrome types, including time in range (TIR), standard deviation of blood glucose (SDBG), mean amplitude of glycemic excursion (MAGE), mean of daily difference (MODD), coefficient of variation (CV), glycosylated hemoglobin (HbA1c), relative appendicular skeletal muscle (RASM), appendicular skeletal muscle mass (ASM) and

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total lean mass (TLM). Compliance was based on TIR $\geq 70\%$. **Results** The TIR compliance rate of Qi and Yin deficiency syndrome group was 46.7%, dryness-heat due to Yin deficiency syndrome group was 30.7%, and damp-heat tapping spleen syndrome group was 47.9%. There was a significant difference in the TIR compliance rate among the three groups ($\chi^2 = 7.145$, $P = 0.028$), and the TIR compliance rate of Qi and Yin deficiency syndrome group and damp-heat tapping spleen syndrome group was significantly higher than that of dryness-heat due to Yin deficiency syndrome group ($P < 0.05$). SDBG, MAGE, MODD and CV in dryness-heat due to Yin deficiency syndrome group were significantly lower than those in Qi and Yin deficiency syndrome group and dryness-heat due to Yin-deficiency syndrome group ($P < 0.05$). In Qi and Yin deficiency syndrome group, ASM was significantly lower than that in other two groups ($P < 0.05$). In dryness-heat due to Yin deficiency syndrome group, RASM was respectively negatively correlated with SDBG ($r = -0.234$, $P = 0.029$), MODD ($r = -0.248$, $P = 0.029$) and CV ($r = -0.355$, $P = 0.001$). **Conclusion** There are differences in blood glucose fluctuation and skeletal muscle content in T2MD patients with different Chinese medicine syndromes types. There is a correlation between blood glucose fluctuations and skeletal muscle content in patients with dryness-heat due to Yin deficiency syndrome.

Keywords: Type 2 diabetes mellitus; Chinese medicine syndrome; Blood sugar fluctuation; Skeletal muscle mass; Qi and Yin deficiency syndrome; Dryness-heat due to Yin deficiency syndrome; Damp-heat tapping spleen syndrome

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2型糖尿病是一组由胰岛素分泌和/或作用缺陷引起的以高血糖为特征的代谢性疾病^[1]。较大的血糖变异性与糖尿病的多种不良终点事件相关,如糖尿病大血管病变^[2-3]、糖尿病微血管病变^[4]、糖尿病周围神经病变^[5]等。骨骼肌占据全身体质量的40%~60%,是主要的葡萄糖处理场所,对全身血糖稳态发挥重要作用^[6]。Schein等^[7]发现对吸气肌肉的训练可降低血糖水平和血糖变异性,说明肌肉对血糖变异性起到了不可忽视的作用。相关研究发现肌量减少导致胰岛素抵抗、糖代谢紊乱,低肌量甚至可作为糖尿病发病的早期预测因子^[8]。

2型糖尿病在中医上属于“消渴病”的范畴,现代医家普遍认为糖尿病病程中血糖波动的根本病位在中焦脾胃^[9],主要病机为脾虚失于散精^[10]。但不同证型之间的血糖波动与骨骼肌含量的差异性及两者相关性研究尚不足。本文通过回顾性研究分析这两者的关系,为临床治疗提供新的参考依据。

1 资料与方法

1.1 一般资料 共纳入2020年9月至2021年9月在上海中医药大学附属曙光医院内分泌科住院的330例2型糖尿病患者。男171例,女159例;年龄63(51,68)岁;身体质量指数(body mass index, BMI)24.60(22.60, 26.90)kg/m²;2型糖尿病病程10.00(3.75, 16.00)年。本研究经上海中医药大学附属曙光医院伦理委员会批准(ChiCTR2000039423)。

1.2 西医诊断标准 参照1999年WHO的2型糖尿病诊断标准^[11],即典型症状加上随机血糖 ≥ 11.1 mmol/L或空腹血糖 ≥ 7.0 mmol/L或口服葡萄糖耐量试验(oral glucose tolerance test, OGTT)2 h血糖 ≥ 11.1 mmol/L,症状不典型需改日复查。

1.3 中医诊断标准 参照中华中医药学会拟定的2007年版《糖尿病中医防治指南》^[12]中消渴病分型。(1)湿热困脾证:形体肥胖,食后腹胀,易汗出,舌红,苔黄腻,脉滑数;(2)阴虚燥热证:口渴引饮,多食易饥,喜冷饮,咽燥,舌红,苔黄燥,脉细数;(3)气阴两虚证:口干渴,多饮,疲倦无力,气短懒言,体形瘦削,舌红少津,苔薄,脉细无力。

1.4 纳入标准 (1)符合上述西医及中医诊断标准;(2)受试期间维持原降糖方案不变;(3)年龄30~75岁;(4)佩戴动态血糖监测系统不低于72 h;(5)监测过程中无糖尿病酮症酸中毒等急性并发症发生。

1.5 排除标准 (1)严重的心、肝、肾功能不全;(2)近3个月发生运动系统疾病处于全身制动状态;(3)近1个月有糖尿病急性并发症及其他急性感染发生;(4)患有精神疾病及其他严重内科疾病。

1.6 研究指标 (1)采用Bio-RADVARIANT II型检测仪统一测定糖化血红蛋白(hemoglobin A1c, HbA1c)。(2)采用动态血糖监测系统(CGMS,美敦力公司,美国)进行连续72 h动态血糖监测,测定血糖波动指标,包括目标范围内时间(time in range, TIR)、血糖变异系数(coefficient of variation, CV)、血

糖标准差 (standard deviation of blood glucose, SDBG)、24 h 平均血糖波动幅度 (mean amplitude of glycemic excursion, MAGE)、日间血糖平均绝对差 (mean of daily difference, MODD)。参照《中国 2 型糖尿病防治指南 (2020 年版)》, 以 TIR ≥ 70% 为已达标。(3) 采用双能 X 线骨密度仪 (Lunar iDXA, GE 公司, 美国) 测定四肢骨骼肌质量 (appendicular skeletal muscle mass, ASM)、总肌肉质量 (total lean mass, TLM)。以四肢骨骼肌质量 / 身高² 计算相对骨骼肌质量指数 (relative appendicular skeletal muscle, RASM)^[13]。

1.7 统计学方法 采用 SPSS 20.0 软件完成统计学分析。计量资料若符合正态分布用 $\bar{x} \pm s$ 表示, 两组间比较用 *t* 检验, 多组比较用单因素方差分析; 若偏态分布用 $M(P_{25}, P_{75})$ 表示, 两组间比较采用 Mann-Whitney *U* 检验, 多重比较采用 Kruskal-Wallis *H* 检验。计数资料用例数 (%) 表示, 组间比较采用 χ^2 检验。若双变量服从正态分布, 则采用 Pearson 相关分析, 若不服从正态分布, 则采用 Spearman 相关分析。 $P < 0.05$ 为差异有统计学意义。

2 结 果

2.1 一般情况 330 例 2 型糖尿病患者中气阴两虚证共 169 例 (51.2%), 阴虚燥热证为 88 例 (26.7%), 湿热困脾证为 73 例 (22.1%)。三组性别构成差异无统计学意义 ($P > 0.05$)。气阴两虚证组年龄和病程大于阴虚燥热证组及湿热困脾证组 ($P < 0.05$), 湿热困脾证组 BMI 高于气阴两虚证组及阴虚燥热证组 ($P <$

0.05)。见表 1。

2.2 不同中医证型间血糖波动指标比较 湿热困脾证组 SDBG、MAGE、MODD、CV 均低于气阴两虚证组及阴虚燥热证组, 差异有统计学意义 ($P < 0.05$)。阴虚燥热证组 HbA1c 高于气阴两虚证组及湿热困脾证组, 差异有统计学意义 ($P < 0.05$)。阴虚燥热证组 SDBG、MAGE、MODD、CV 与气阴两虚证组比较, 差异无统计学意义 ($P > 0.05$)。三组不同证型 TIR 达标率比较, 差异有统计学意义 ($P < 0.05$), 且湿热困脾证组和气阴两虚证组 TIR 达标率大于阴虚燥热证组, 差异具有统计学意义 ($P < 0.05$)。见表 2。

2.3 不同中医证型间骨骼肌含量比较 三组不同证型 TLM 比较, 差异无统计学意义 ($P > 0.05$)。气阴两虚证组 ASM 低于阴虚燥热证组及湿热困脾证组, 差异有统计学意义 ($P < 0.05$); 阴虚燥热证组 ASM 与湿热困脾证组差异无统计学意义 ($P > 0.05$)。湿热困脾证组 RASM 高于气阴两虚证组, 差异有统计学意义 ($P < 0.05$); 气阴两虚证组 RASM 与阴虚燥热证组差异无统计学意义 ($P > 0.05$)。见表 3。

2.4 不同证型血糖波动指标与 RASM 的相关性 气阴两虚证组中, RASM 与 TIR、SDBG、MAGE、MODD、CV 无显著相关性 ($P > 0.05$)。阴虚燥热证组中, RASM 与 SDBG ($r = -0.234, P = 0.029$)、MODD ($r = -0.248, P = 0.029$)、CV ($r = -0.355, P = 0.001$) 均呈负相关, 与 TIR、MAGE 均无显著相关性 ($P > 0.05$)。湿热困脾证组中, RASM 与 TIR、SDBG、MAGE、MODD、CV 均无显著相关性 ($P > 0.05$)。见表 4。

表 1 不同中医证型糖尿病患者一般资料比较 [$M(P_{25}, P_{75})$]

Tab. 1 Comparison of general data of diabetes patients with different Chinese medicine syndromes [$M(P_{25}, P_{75})$]

证型	例数	性别(例)		年龄(岁)	病程(年)	BMI(kg/m ²)
		男	女			
气阴两虚证	169	90	79	65.00(59.00,70.00)	15.00(10.00,20.00)	24.20(22.60,25.80)
阴虚燥热证	88	44	44	57.00(47.00,64.00) ^a	2.00(0.33,7.75) ^a	24.30(22.05,26.68)
湿热困脾证	73	37	36	62.00(49.00,47.00) ^a	6.00(2.00,11.00) ^{ab}	26.90(24.12,28.96) ^{ab}
χ^2/H 值		0.294		32.486	128.304	24.420
<i>P</i> 值		0.863		<0.001	<0.001	<0.001

注: 与气阴两虚证组比较, ^a $P < 0.05$; 与阴虚燥热证组比较, ^b $P < 0.05$ 。

表 2 不同中医证型间血糖波动指标比较 [$M(P_{25}, P_{75})$]

Tab. 2 Comparison of blood glucose fluctuation indicators among different Chinese medicine syndromes [$M(P_{25}, P_{75})$]

证型	例数	SDBG (mmol/L)	MAGE (mmol/L)	MODD (mmol/L)	CV (%)	HbA1c (%, $\bar{x} \pm s$)	TIR 达标 [例(%)]
气阴两虚证	169	2.00(1.55,2.46)	3.68(2.85,4.60)	1.67(1.41,2.33)	23.72(19.28,27.53)	8.57±1.81	79(46.7)
阴虚燥热证	88	2.10(1.63,2.82)	3.98(3.15,4.90)	1.93(1.36,2.69)	23.96(19.70,28.90)	9.77±2.52 ^a	27(30.7) ^a
湿热困脾证	73	1.51(1.22,1.93) ^{ab}	3.04(2.37,4.11) ^{ab}	1.45(1.17,1.18) ^{ab}	18.82(15.47,23.09) ^{ab}	8.20±1.63 ^b	35(47.9) ^b
$H/F/\chi^2$ 值		23.201	14.378	14.462	25.559	14.828	7.145
<i>P</i> 值		<0.001	0.001	0.001	<0.001	<0.001	0.028

注: 与气阴两虚证组比较, ^a $P < 0.05$; 与阴虚燥热证组比较, ^b $P < 0.05$ 。

表3 不同中医证型间骨骼肌含量比较 ($\bar{x} \pm s$)**Tab. 3 Comparison of skeletal muscle content among different Chinese medicine syndromes ($\bar{x} \pm s$)**

证型	例数	TLM [kg, M (P_{25}, P_{75})]	ASM (kg)	RASM (kg/m ²)
气阴两虚证	169	42.58(37.29,48.74)	18.27±4.16	6.69±1.00
阴虚燥热证	88	46.00(39.17,50.24)	19.42±4.36 ^a	6.94±1.20
湿热困脾证	73	44.25(37.84,52.91)	19.52±4.68 ^a	7.11±1.22 ^a
H/F 值		4.079	3.155	4.064
P 值		0.130	0.044	0.018

注:与气阴两虚证组比较,^a $P < 0.05$;与阴虚燥热证组比较,^b $P < 0.05$ 。

表4 不同中医证型间血糖波动与 RASM 的相关性**Tab. 4 Correlation between blood glucose fluctuations and RASM among different Chinese medicine syndromes**

证型	TIR	SDBG	MAGE	MODD	CV	
气阴两虚证	r 值 P 值	0.117 0.129	-0.152 0.050	-0.152 0.050	-0.133 0.104	-0.082 0.290
阴虚燥热证	r 值 P 值	0.051 0.637	-0.234 0.029	-0.211 0.050	-0.248 0.029	-0.355 0.001
湿热困脾证	r 值 P 值	0.095 0.423	-0.182 0.123	-0.139 0.240	-0.097 0.446	-0.108 0.364

3 讨论

消渴之名,首见于《黄帝内经》。《素问·奇病论》指出“此肥美之所发也,此人必数食甘美而多肥也,肥者令人内热,甘者令人中满,故其气上溢,转为消渴”。嗜食肥甘厚味,久而酿生湿热,碍胃滞脾,脾失健运,导致精微无法正常输布,血糖波动随之出现^[14]。同血糖波动的主要病机,即脾失散精类似^[15-16]。《四圣心源》言:“肌肉者,脾土之所生也,脾气盛则肌肉丰满而充实。”肌肉的丰满强壮均依赖于脾气的健运及精微物质的充养。故中医认为肌肉的强壮有力,丰满健硕也与脾的功能状态相关^[17-18]。

为研究不同中医证型2型糖尿病患者骨骼肌和血糖波动的关系,本研究筛选并纳入330例2型糖尿病患者,发现不同证型间长期和短期血糖波动指标及骨骼肌含量均存在显著差异。气阴两虚证及阴虚燥热证长期血糖波动均较大。《医学刍言》中提到:“消渴,火证也。”燥热之邪稽留中焦脾胃,出现多食且消瘦,热为阳邪,易耗津液,灼伤人体气血津液,久则气阴两虚,渐为虚热。现代医学“糖高不离火”的思想与之相符^[19]。

本研究也发现气阴两虚证及阴虚燥热证患者骨骼肌含量较少,有研究也发现脾虚大鼠骨骼肌线粒体病变明显^[20],通过四君子汤^[20]或补中益气汤^[21]等健脾益气治疗后,大鼠脾虚症状消失,损伤的线粒体结构和功能恢复正常。相关研究也显示,年龄及糖尿病

病程是骨骼肌含量减少的主要影响因素^[22],本研究中发现气阴两虚证组年龄较大和病程较长。

结合现代医学来看,由脾主导的糖调节路径也有骨骼肌的参与^[23]。骨骼肌是胰岛素作用的靶器官之一,也是血糖等精微物质的储存池,与血糖稳态密切相关^[24]。中医认为脾功受损,导致人体气血阴阳、津液失衡,阴成形,阳化气,在宏观上会出现消瘦等骨骼肌丢失的表现,在微观上可能出现血糖波动明显。在本研究中,湿热困脾证组及气阴两虚证组血糖波动和RASM 无明显相关性,阴虚燥热证组这两者呈显著负相关。

综上所述,不同证型2型糖尿病患者的血糖波动指标和骨骼肌含量均有差异,且气阴两虚证和阴虚燥热证的短期血糖波动指标和骨骼肌含量有相关性。这提示在诊治这两种证型的2型糖尿病患者时,可以从健脾的角度出发,增加骨骼肌含量,以此达到减少血糖波动的目的^[25]。本研究结果仅说明2型糖尿病患者血糖波动情况与骨骼肌含量有关,但具体机制尚未阐明,后续可以进一步在临床及动物实验上探究。
利益冲突 无

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