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男性痛风患者血清尿酸水平与载脂蛋白B的关系研究

李　洁[1]，杨玉媛[2]，王颜刚[1]，李海铭[1]，王忠超[1*]

[1]青岛大学附属医院内分泌与代谢性疾病科，山东　青岛
[2]青岛大学附属医院老年医学科，山东　青岛
Email: *1248580706@qq.com

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摘　要

目的：探讨男性痛风(Gout)患者血清尿酸(SUA)水平与载脂蛋白B (ApoB)的关系。方法：回顾性选取2019年1月1日至2021年3月31日于青岛大学附属医院内分泌与代谢性疾病科就诊的住院患者以及门诊患者，纳入符合条件的男性痛风患者73例。根据《中国高尿酸血症与痛风诊疗指南(2019)》要求，将患者分为SUA达标组(19例)和SUA升高组(54例)，比较组间差异。采用Pearson相关分析SUA和ApoB的相关性，利用logistic回归模型进行相关危险因素分析。结果：与SUA达标组相比，SUA升高组ApoB的平均水平升高，差异有统计学意义($P < 0.05$)。Pearson相关性分析显示ApoB与SUA呈正相关。单因素logistic回归分析显示，男性痛风患者SUA水平升高是ApoB的危险因素($OR = 0.986$, 95% CI 0.979~0.993, $P < 0.001$)；当校正年龄、空腹血糖(FBG)、身体质量指数(BMI)等因素后，两者关系仍然成立。结论：男性痛风患者SUA与ApoB相关，当SUA水平升高时，可导致ApoB水平升高。

关键词

男性，痛风，血清尿酸，载脂蛋白B

Study on the Relationship between Serum Uric Acid Level and Apolipoprotein B in Male Patients with Gout

Jie Li[1], Yuyuan Yang[2], Yangang Wang[1], Haiming Li[1], Zhongchao Wang[1*]

*通讯作者。

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[1]Department of Endocrinology and Metabolism, The Affiliated Hospital of Qingdao University, Qingdao Shandong
[2]Department of Geriatrics, The Affiliated Hospital of Qingdao University, Qingdao Shandong
Email: *1248580706@qq.com

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Abstract

Objective: To explore the relationship between serum uric acid (SUA) and apolipoprotein B (Apo B) in male gout patients. Methods: A total of 73 eligible male patients with gout were retrospectively selected from the inpatients and outpatients who were admitted to the Department of Endocrinology and Metabolism Diseases of the Affiliated Hospital of Qingdao University on January 1, 2019 and March 31, 2021. According to the requirements of the "Guidelines for the Diagnosis and Treatment of Hyperuricemia and Gout in China (2019)", patients were divided into the SUA standard group (19 cases) and the SUA elevated group (54 cases), and the differences between the groups were compared. Pearson correlation analysis was used to analyze the correlation between SUA and ApoB, and logistic regression model was used to analyze related risk factors. Results: Compared with the SUA level up to standard group, the average level of ApoB in the high SUA group increased, and the difference was statistically significant (P < 0.05). Pearson correlation analysis showed that ApoB was positively correlated with SUA. Univariate logistic regression analysis showed that elevated SUA level was a risk factor for ApoB in male patients with gout (OR = 0.986, 95% CI 0.979~0.993, P < 0.001). After adjusting for age, fasting blood glucose (FBG), body mass index (BMI) and other factors, the relationship still held. Conclusion: SUA is related to ApoB in male patients with gout. When the level of SUA increases, it can cause the level of ApoB to increase.

Keywords

Male, Gout, Serum Uric Acid, Apolipoprotein B

1. 引言

近年来，随着人们生活水平的提高和饮食结构的改变，痛风(Gout)的患病率在世界范围内逐年上升，成为既糖尿病之后又一常见的代谢性疾病[1] [2] [3]。而且 Gout 的发生有着明显的性别差异，男性的患病率明显高于女性[4] [5]。研究显示，与无症状高尿酸血症患者相比，Gout 患者更容易合并血脂代谢异常，进而增加了痛风患者罹患心脑血管疾病的风险[6]；同时，血脂异常也是导致 Gout 发作的危险因素。因此，针对 Gout 患者，不仅要关注其血清尿酸(SUA)水平，同时也要兼顾患者血脂变化。一直以来，血脂中低密度脂蛋白(LDL)是公认的导致发生动脉粥样硬化发生、发展的独立危险因素；然而人们虽然关注了 LDL 的水平，却往往忽视了载脂蛋白 B (ApoB)的变化，它与 LDL 一样，可以促进动脉粥样硬化性心血管疾病(ASCVD)的发生，但是在预测心脑血管疾病方面优于 LDL [7]。近些年来，针对 ApoB 的研究越来越多，本研究将探讨男性痛风患者的 SUA 与 ApoB 的关系。

2. 对象和方法

2.1. 研究对象

回顾性选取2019年1月1日至2021年3月31日于青岛大学附属医院内分泌与代谢性疾病科就诊的住院患者以及门诊患者，纳入符合条件的男性痛风患者 74 例，研究对象均符合美国风湿病协会制定的2015 年痛风分类标准[8]。排除标准：1) 既往诊断为糖尿病、甲状腺功能减退、高脂血症、肾病综合征等疾病；2) 既往应用过激素、化疗药物、免疫抑制剂以及他汀类调脂药等药物；3) 严重的心力衰竭(纽约分级 III 级或 IV 级)、肝功能不全[谷丙转氨酶(ALT)、谷草转氨酶(AST)升高超过正常水平的3倍]、严重的肾功能不全；4) 基线资料不全的患者。

2.2. 研究方法

男性痛风患者的一般资料如年龄、身高、体重、BMI 等资料通过电子病例查阅获取；实验室检验指标如 SUA、FBG、甘油三酯(TG)、总胆固醇(TC)、高密度脂蛋白(HDL)、载脂蛋白 A (ApoA)、脂蛋白 A [LP(a)]、ApoB、LDL、游离脂肪酸、ALT、AST 等均由患者在禁食 8 h 后，次日清晨抽取静脉血测得，所有检验结果均由我院检验科完成。

2.3. 研究分组

根据《中国高尿酸血症与痛风诊疗指南(2019)》：所有痛风患者终生血尿酸水平控制范围为 240~420 μmol/L，将男性痛风患者分为 SUA 水平达标组(SUA ≤ 420 μmol/L)和 SUA 升高组(SUA > 420 μmol/L)。

2.4. 统计分析

采用 SPSS 26.0 统计软件对数据进行分析：符合正态分布的计量资料用均数 ± 标准差($\bar{x} \pm s$)表示，组间比较采用独立样本 t 检验；偏态分布或方差不齐的计量资料用中位数(上、下四分位数)表示，组间比较采用 Mann-Whitney U 检验；计数资料采用百分比(%)的形式表示，组间比较采用 x^2 检验；采用 Pearson 相关性分析进行 SUA 和 ApoB 相关性检验；采用 logistic 回归模型进行相关危险因素分析。所有分析采用双侧检验，以 $P < 0.05$ 为差异有统计学意义。

3. 结果

3.1. 一般临床特征

共纳入74例男性痛风患者，平均年龄为(40.78 ± 13.66)岁；其中SUA水平升高组53例，平均年龄(38.52 ± 11.91)岁；SUA 水平达标组 19 例，平均年龄(47.21 ± 16.396)岁。其中，SUA 水平升高组的年龄小于 SUA 达标组的年龄($P < 0.05$)，但 TG、LDL、ApoB、ApoB/ApoA、LP(a)的平均水平高于血清水平达标组($P < 0.05$)，两组间 BMI、FBG、ALT、AST、TC、HDL、ApoA、游离脂肪酸差异无统计学意义($P > 0.05$)。见表 1。

3.2. SUA 水平与 Apo B 的相关性分析

Pearson 相关性分析显示 ApoB 与 SUA 水平显著相关，成正相关；而且在控制 BMI、FBG、TG、TC、HDL、ApoA、LP(a)、游离脂肪酸、ALT、AST 等变量后，ApoB 与 SUA 仍具有相关性，且 $P < 0.05$。见表 2。

Table 1. Baseline characteristics of the study population with different SUA levels cases (%), $\bar{x} \pm s$
表 1. 不同 SUA 水平研究人群的基线特征例(%)，$\bar{x} \pm s$

项目	总体	SUA (μmol/L)		P 值
		升高组	达标组	
一般资料				
例数	73 (100%)	54 (73.97%)	19 (26.03%)	
年龄/(岁)	40.78 ± 13.66	38.52 ± 11.91	47.21 ± 16.396	0.016
BMI/(Kg/m^2)	28.56 ± 3.81	29.06 ± 3.77	27.12 ± 3.65	0.056
临床指标				
FBG/(mmol/L)	4.91 ± 0.67	4.94 ± 0.70	4.84 ± 0.55	0.597
ALT/(U/L)	46.16 ± 36.22	47.06 ± 34.51	43.63 ± 41.62	0.726
AST/(U/L)	25.05 ± 14.66	24.93 ± 12.56	25.42 ± 19.88	0.900
TC/(mmol/L)	4.86 ± 0.95	5.12 ± 0.77	3.91 ± 0.75	0.193
TG/(mmol/L)	1.80 ± 0.78	1.87 ± 0.70	1.60 ± 0.96	<0.001
LDL/(mmol/L)	3.21 ± 0.72	3.46 ± 0.63	2.50 ± 0.48	<0.001
HDL/(mmol/L)	1.06 ± 0.25	1.08 ± 0.26	0.96 ± 0.17	0.053
ApoA/(g/L)	1.16 ± 0.23	1.18 ± 0.24	1.09 ± 0.21	0.150
ApoB/(g/L)	1.08 ± 0.23	1.16 ± 0.20	0.85 ± 0.14	<0.001
ApoB/ApoA	1.01 ± 0.45	1.08 ± 0.48	0.80 ± 0.21	0.019
LP(a)/(mg/L)	253.72 ± 279.97	277.51 ± 314.92	186.09 ± 122.45	0.023
游离脂肪酸(mmol/L)	0.37 ± 0.15	0.39 ± 0.15	0.32 ± 0.12	0.059

Table 2. Pearson correlation analysis between ApoB and SUA
表 2. ApoB 与 SUA Pearson 相关分析

控制变量	r 值	P 值
	0.626	<0.001
BMI	0.616	<0.001
FBG	0.628	<0.001
TG	0.603	<0.001
TC	0.283	0.016
HDL	0.624	<0.001
ApoA	0.625	<0.001
ApoB/ApoA	0.523	<0.001
LP(a)	0.621	<0.001
ALT	0.637	<0.001
AST	0.665	<0.001
游离脂肪酸	0.614	<0.001

3.3. Logistic 回归分析

单因素 logistic 回归分析显示，男性痛风患者 SUA 水平升高是 ApoB 的危险因素(OR = 0.986, 95% CI 0.979~0.993, P < 0.001)。多因素 logistic 回归校正年龄、FBG、TG、HDL、ApoA、LP(a)、ALT、AST、

BMI、游离脂肪酸后，SUA 水平仍是 ApoB 的危险因素(OR = 0.986, 95% CI 0.978~0.994, P = 0.001)。见表 3。

Table 3. Logistic regression between SUA and ApoB
表 3. SUA 与 ApoB 的 Logistic 回归

项目	OR	95% CI	P 值
模型 1			
SUA	0.986	0.979~0.993	<0.001
模型 2			
年龄	1.011	0.968~1.056	0.614
FBG	0.898	0.392~2.058	0.798
TG	0.707	0.337~1.483	0.359
HDL	0.902	0.106~7.695	0.925
ApoA	1.528	0.139~16.782	0.729
LP(a)	1.000	0.998~1.002	0.842
ALT	0.990	0.974~1.006	0.219
AST	0.974	0.935~1.015	0.210
BMI	0.905	0.782~1.047	0.178
游离脂肪酸	1.197	0.027~53.591	0.926
SUA	0.986	0.978~0.994	0.001

4. 讨论

Gout 是一种慢性炎症性疾病，以嘌呤代谢失衡为特征，由于持续升高的 SUA 超过其在血液或组织中的饱和度，导致在关节局部形成尿酸钠晶体并沉积，表现为周围关节滑膜炎急性自限性的反复发作，疼痛在几天或几周内可缓解[9] [10] [11]。长期的尿酸钠晶体沉积可致痛风石形成，导致关节损伤和畸形，最终引起关节功能障碍。研究显示，SUA 升高不仅是痛风发作的危险因素，并可引起痛风患者机体血糖、血压、血脂等代谢异常，增加痛风患者罹患心脑血管疾病的风险。此外，多篇文章也报导过，SUA 控制不佳，可引起血脂紊乱，Ali N 等一项研究表明，SUA 与 TG、TC、LDL 呈正相关；此外；Tao M 等也报导过，SUA 与血脂呈正相关[12] [13]。

多数的研究往往关注了 SUA 与 TG、TC、LDL 以及 HDL 之间的关系，而未加阐释 SUA 与 ApoB 的关系。ApoB 在血脂中发挥着重要的作用，它是乳糜微粒(CM)、LDL、极低密度脂蛋白(VLDL)等的载体。同时，它是所有致动脉粥样硬化或者潜在致动脉粥样硬化颗粒的组成成分，包括 VLDL、中密度脂蛋白(IDL)、LDL 等，每个颗粒中含有 1 分子 ApoB；因 LDL 占绝大多数，大约 90%的 ApoB 分布在 LDL 中，可以说，ApoB 可代表 LDL 的水平，但是 ApoB 比 LDL 能更好地预测心血管危险[14] [15] [16]。

本研究中男性痛风患者 SUA 水平升高组 ApoB 的平均水平较 SUA 达标组平均水平高，而且差异有统计学意义(P < 0.001)；Pearson 相关性分析显示 ApoB 与 SUA 水平呈正相关；单因素 logistic 回归分析显示，SUA 水平是 ApoB 的危险因素，当校正年龄、FBG、BMI 等因素后，两者关系仍然成立。其可能的机制是，SUA 水平升高时会增加脂肪细胞、血管平滑肌细胞等氧化应激，使得活性氧(ROS)产生增加，ROS 介导了胰岛素抵抗，从而引起血脂代谢异常[17] [18]。本研究中男性痛风患者 SUA 升高组的平均年龄较 SUA 达标组低，两者呈负相关，考虑男性在青年时期本就是痛风患者的高危人群，且有不良饮食习

惯相关；当不良饮食习惯得以改正，随着年龄增长，痛风发病率反而呈下降趋势[19]。

综上所述，在男性痛风患者中，SUA 控制不佳与血脂紊乱明显相关性，当 SUA 水平升高时，可引起 ApoB 异常，其水平升高更能预示着罹患心脑血管的风险增加。因此，针对男性痛风患者，监测 SUA 以及 ApoB 有明显的临床意义，严格控制 SUA 水平，可减少发生血脂紊乱的风险，进而降低罹患心脑血管等并发症的风险。

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