

中青年冠心病患者中血清尿酸水平与冠状动脉狭窄程度的关系： 一项单中心回顾性研究

李子文 蔺雅娟 樊瑞 夏云龙 杨晓蕾

(大连医科大学附属第一医院心内科, 辽宁 大连 116011)

【摘要】目的 通过回顾性研究分析中青年冠心病患者中影响冠状动脉血管狭窄程度的临床因素,探讨中青年冠心病患者入院时血清尿酸(SUA)水平与冠状动脉血管狭窄程度之间的流行病学关系。**方法** 连续入选 2010 年 1 月—2020 年 6 月于大连医科大学附属第一医院就诊的中青年冠心病患者,年龄 20~65 岁,共计 8 644 例,排除无 SUA 值、高血压、糖尿病、痛风、肿瘤、肾功能不全、心力衰竭等影响 SUA 水平的患者,最终纳入中青年冠心病患者共 3 957 例。根据冠状动脉造影结果分为重度狭窄组(任何一支冠状动脉狭窄程度 $\geq 75\%$)($n=1\ 016$)和轻中度狭窄组($n=2\ 941$)。比较两组患者的临床特点及冠状动脉造影结果,分析 SUA 水平是否对冠状动脉血管狭窄程度产生影响。**结果** (1)基线资料显示冠状动脉血管重度狭窄组患者的 SUA 水平为 360(307~423) $\mu\text{mol/L}$,显著高于轻中度狭窄组 335(279~399) $\mu\text{mol/L}$ ($P<0.001$);且 Spearman 相关分析显示,SUA 水平与冠状动脉血管狭窄程度之间呈正相关($r=0.129$, $P<0.001$);应用二元 logistic 回归分析,以 SUA Q1 分层为参考,随着 SUA 水平的升高,冠状动脉血管重度狭窄的风险升高,Q3、Q4 的校正 OR 值分别为 1.267 与 1.372 倍。(2)ROC 曲线示 20~35 岁冠心病人群中,SUA 对重度冠状动脉血管狭窄具有较高的预测价值($AUC=0.741$,灵敏度 75.5%,特异度 65.5%)。且 $SUA>422.5\ \mu\text{mol/L}$ 比 $SUA\leq 422.5\ \mu\text{mol/L}$ 患者重度狭窄的患病率高(44.2% vs 11.9%, $P<0.001$)。(3)对 20~35 岁人群进行多因素二元 logistic 回归分析显示, $SUA>422.5\ \mu\text{mol/L}$ 的患者冠状动脉血管重度狭窄的风险是 $SUA\leq 422.5\ \mu\text{mol/L}$ 者的 5.8 倍($OR=5.8$,95% $CI\ 2.020\sim 16.653$, $P=0.001$)。**结论** SUA 水平与中青年冠心病患者冠状动脉狭窄程度呈显著相关性,患者 SUA 水平越高,冠状动脉血管重度狭窄的风险越大;在 20~35 岁冠心病人群中,SUA 可能对冠心病患者冠状动脉狭窄程度具有较高的预测价值。

【关键词】 尿酸;冠心病;年龄

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Relationship Between Serum Uric Acid Level and Coronary Artery Stenosis in Young and Middle-Aged Patients with Coronary Heart Disease: A Single-Center Retrospective Study

LI Ziwen, LIN Yajuan, FAN Rui, XIA Yunlong, YANG Xiaolei

(Department of Cardiology, The First Affiliated Hospital of Dalian Medical University, Dalian 116011, Liaoning, China)

【Abstract】 Objective Through a large sample retrospective study, to examine the clinical factors influencing the extent of coronary vascular stenosis in young and middle-aged patients with coronary heart disease, and to investigate the effect of serum uric acid (SUA) level on the extent of coronary vascular stenosis. **Methods** A total of 8 644 young and middle-aged patients with coronary heart disease, aged 20~65 years, were admitted at The First Affiliated Hospital of Dalian Medical University from January 2010 to June 2020. After excluding patients without SUA value, and patients with hypertension, diabetes, gout, tumor, renal function deficiency, and heart failure, finally 3 957 young and middle-aged patients were included. According to coronary angiography, they were divided into severe stenosis group ($n=1\ 016$) and mild-to-moderate stenosis group ($n=2\ 941$). The clinical characteristics and the results of coronary angiography were compared between the two groups, and whether the SUA level had an effect on the extent of coronary artery stenosis was analyzed. **Results** (1) The baseline data shows that the SUA level of patients with severe coronary artery stenosis group was 360 (307~423) $\mu\text{mol/L}$, which is significantly higher than that of the mild-to-moderate stenosis group 335 (279~399) $\mu\text{mol/L}$ ($P<0.001$); and Spearman correlation analysis shows that there is a positive correlation between SUA level and coronary artery stenosis ($r=0.129$, $P<0.001$); binary logistic regression analysis shows, compared with the first quartile of SUA, as the level of SUA increasing, the risk of severe coronary artery stenosis is increased, and the adjusted OR values of

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通信作者:杨晓蕾, E-mail: yangxl1012@yeah.net

Q3, and Q4 were 1.267 and 1.372, respectively. (2) ROC curve shows that in patients with coronary heart disease aged 20 ~ 35 years, SUA has a high predictive value for severe coronary artery stenosis ($AUC = 0.741$, sensitivity 75.5%, specificity 65.5%), and the prevalence of severe stenosis is higher in patients with $SUA > 422.5 \mu\text{mol/L}$ than that with $SUA \leq 422.5 \mu\text{mol/L}$ (44.2% vs 11.9%, $P < 0.001$). (3) Multivariate logistic regression analysis of 20 ~ 35 years old patients shows that the risk of severe coronary artery stenosis in patients with $SUA > 422.5 \mu\text{mol/L}$ was 5.8 times than those with $SUA \leq 422.5 \mu\text{mol/L}$ ($OR = 5.8$, 95% CI 2.020 ~ 16.653, $P = 0.001$). **Conclusion** SUA levels are significantly correlated with the extent of coronary artery stenosis in young and middle-aged patients with coronary heart disease, and patients with higher SUA has higher risk association of severe coronary artery stenosis; among 20 to 35 years old people with coronary heart disease, SUA may have a higher predictive value for the extent of coronary artery stenosis.

[Key words] Uric acid; Coronary heart disease; Age

冠状动脉粥样硬化性心脏病 (coronary heart disease, CHD) 是全球死亡的主要原因, 在亚洲国家, 它的发病率和死亡率高于西方国家^[1-2]。既往的流行病学数据大多来自老年人 (>65 岁), 但由于肥胖以及不良生活方式, 导致 CHD 的发病率在中青年患者中迅速增长^[3], Framingham 心脏研究曾报告了 <55 岁患者的心肌梗死 (myocardial infarction, MI) 10 年发病率, 男性为 51.1/1 000, 女性为 7.4/1 000^[4], 然而对于 ≤ 65 岁的中青年患者 CHD 和 MI 的文献是不足的。并且 MI 的后果可能是毁灭性的, 尤其对中青年患者, 因为它对患者的心理、工作能力和社会经济负担有更大的潜在影响。既往研究指出年轻和年长 MI 患者之间存在的差异, 与老年 MI 患者相比, 年轻 MI 患者的男性占比更大, 吸烟率、高脂血症发生率更高, CHD、糖尿病和高血压病史的发生率更低, 并且该类患者的预后相对老年患者更好^[5-8], 所以对该类 CHD 患者的危险因素评估势在必行。

尿酸是人体内嘌呤代谢的终产物, 大部分经肾脏排出体外。当体内尿酸生产过剩或排泄不足时将会引起高尿酸血症, 一般认为血清尿酸 (serum uric acid, SUA) 水平: 男性 $\geq 420 \mu\text{mol/L}$ (7 mg/dL)、女性 $\geq 360 \mu\text{mol/L}$ (6 mg/dL) 为高尿酸血症。近年来研究发现高尿酸血症还可能与高血压、CHD 等心血管疾病等的发生发展密切相关^[9-11], 在中国 CHD 为心血管疾病发病率及死亡率高的主要病因^[12]。高尿酸血症被广泛认为是一种独立的风险因素, 对 CHD 有因果关系^[13-16]。相反, 一些报道^[17]对 SUA 和 CHD 之间的直接积极关系产生了怀疑, 因为它与许多传统的 CHD 危险因素, 如高血压、糖尿病、肥胖和高脂血症^[18-20]等密切相关, 所以认为 SUA 对于 CHD 更可能是一种间接关系或旁观者。因此, SUA 在一般 CHD 人群中的作用尚未达成共识, 而在中青年患者中则研究更少。在本研究中, 探讨了中国中青年 (≤ 65 岁) CHD 人群中 SUA 水平与冠状动脉狭窄程度之间的流行病学联系。

1 资料与方法

1.1 研究对象

本研究为回顾性观察性研究, 连续纳入了 2010 年 1 月—2020 年 6 月于大连医科大学附属第一医院就诊的 20 ~ 65 岁 CHD 患者 ($n = 8\ 644$), 所有纳入的患者均符合 CHD 诊断标准: (1) 心绞痛或 MI 发作症状; (2) 心电图示心肌缺血改变; (3) 冠状动脉造影示左主干、左前降支、左回旋支或右冠状动脉存在狭窄。排除无 SUA 检验值的患者。为了更清晰探讨 SUA 与 CHD 之间的关系, 进一步排除合并有高血压、糖尿病、慢性肾功能不全、痛风、心力衰竭以及肿瘤等可能影响 SUA 水平的患者, 最终 3 957 例中青年 CHD 患者被纳入研究, 根据冠状动脉造影结果分为重度狭窄组 ($n = 1\ 016$) 和轻中度狭窄组 ($n = 2\ 941$)。

1.2 收集资料

患者一般资料、冠状动脉造影及经皮冠状动脉介入治疗 (percutaneous coronary intervention, PCI) 记录、实验室检查结果, 如 SUA、低密度脂蛋白胆固醇 (low-density lipoprotein cholesterol, LDL-C)、高密度脂蛋白胆固醇 (high-density lipoprotein cholesterol, HDL-C)、总胆固醇、甘油三酯、血糖、血清肌酐等从病历系统收集, 对于 SUA、血清肌酐等数值选取行冠状动脉造影和介入手术之前的检验数值, 患者均已签署知情同意书且研究已通过医院伦理委员会审核, 以上资料均来源于大连医科大学病历系统。

1.3 临床定义

入组患者均常规进行冠状动脉造影, 由该院经验丰富的介入心脏病医师采用 Seldinger 法穿刺桡动脉或者股动脉并采用 Judkins 法行左、右冠状动脉造影。应用目测法分别对左主干、左前降支, 左回旋支、右冠状动脉及其分支血管的狭窄程度进行评估分析。轻中度狭窄主要是指患者 3 支冠状动脉, 有 1 支或者多支出现了狭窄, 其狭窄的最大直径 $\leq 75\%$ 。重度狭窄被定义为至少有 1 支冠状动脉狭窄 $> 75\%$ 。

1.4 统计学分析

采用 SPSS 22.0 统计软件进行统计分析。计量资料符合正态分布的描述为平均值 \pm 标准差,组间比较采用 Student's *t* test;非正态分布计量资料描述为中位数(四分位数间距),组间比较采用非参数检验(Mann-Whitney *U* 检验);计数资料以 $n(\%)$ 表示,比较采用卡方检验或 Fisher 确切概率检验。相关性分析采用 Spearman 相关性分析,单因素及多因素 logistic 回归分析用来探讨相关危险因素,并根据 OR 值预测疾病发生的概率,ROC 曲线用于评价预测价值。 $P < 0.05$ 为差异具有统计学意义。

2 结果

2.1 重度狭窄组与轻中度狭窄组一般资料统计分析

本研究共纳入了 3 957 例,其中重度狭窄组共 1 016 例,轻中度狭窄组共 2 941 例。两组间基线资料的比较如表 1 所示,重度狭窄组与轻中度狭窄组在年龄、性别、吸烟史、饮酒史、SUA、空腹血糖、肌酐、肌酸激酶、肌钙蛋白 I 和 HDL-C 等指标间差异具有统计学意义($P < 0.01$)。Spearman 相关分析显示(表 2),冠状动脉狭窄程度与 SUA 水平呈正相关($r = 0.129$),且差异有统计学意义($P < 0.001$)。

表 1 重度狭窄组与轻中度狭窄组一般资料统计分析

变量	重度狭窄组($n = 1\ 016$)	轻中度狭窄组($n = 2\ 941$)	<i>P</i> 值
年龄/岁	53.230 \pm 8.468	52.700 \pm 7.713	0.007
男性[$n(\%)$]	901(88.7%)	1 996(67.9%)	<0.001
吸烟史[$n(\%)$]	259(29.8%)	645(24.5%)	<0.001
饮酒史[$n(\%)$]	583(60.7%)	1 173(42.1%)	<0.001
BMI/($\text{kg} \cdot \text{m}^{-2}$)	26.725 (24.160 ~ 29.710)	26.240 (23.730 ~ 29.160)	0.005
LDL-C/($\text{mmol} \cdot \text{L}^{-1}$)	2.193 \pm 0.803	2.199 \pm 0.819	0.931
HDL-C/($\text{mmol} \cdot \text{L}^{-1}$)	1.245 \pm 0.334	1.278 \pm 0.928	0.046
总胆固醇/($\text{mmol} \cdot \text{L}^{-1}$)	5.175 \pm 1.635	5.049 \pm 1.557	0.024
甘油三酯/($\text{mmol} \cdot \text{L}^{-1}$)	1.480(0.960 ~ 2.508)	1.410(0.940 ~ 2.350)	0.178
SUA/($\mu\text{mol} \cdot \text{L}^{-1}$)	360(307 ~ 423)	335(279 ~ 399)	<0.001
肌酐/($\mu\text{mol} \cdot \text{L}^{-1}$)	70(62 ~ 78)	66(57 ~ 76)	<0.001
肌钙蛋白 I/($\text{ng} \cdot \text{mL}^{-1}$)	0.017(0.005 ~ 13.093)	0.006(0.001 ~ 0.009)	<0.001
空腹血糖/($\text{mmol} \cdot \text{L}^{-1}$)	5.050(4.603 ~ 5.680)	4.960(4.540 ~ 5.430)	<0.001
NLR	3.012 \pm 2.966	2.269 \pm 2.668	<0.001

注: BMI: 体质指数; NLR: 中性粒细胞淋巴细胞计数比。

表 2 冠状动脉狭窄程度与各危险因素之间相关性分析

变量	冠状动脉狭窄程度	
	<i>r</i> 值	<i>P</i> 值
SUA	0.129	<0.001
年龄/岁	0.043	0.007
性别	-0.205	<0.001
吸烟史	0.154	<0.001
饮酒史	0.037	0.020
BMI/($\text{kg} \cdot \text{m}^{-2}$)	0.045	0.005
HDL-C/($\text{mmol} \cdot \text{L}^{-1}$)	0.032	0.046
总胆固醇/($\text{mmol} \cdot \text{L}^{-1}$)	0.036	0.024
肌酐/($\mu\text{mol} \cdot \text{L}^{-1}$)	0.120	<0.001
肌钙蛋白 I/($\text{ng} \cdot \text{mL}^{-1}$)	0.209	<0.001
空腹血糖/($\text{mmol} \cdot \text{L}^{-1}$)	0.060	<0.001
NLR	0.176	<0.001

注: BMI: 体质指数; NLR: 中性粒细胞淋巴细胞计数比。

2.2 冠状动脉重度狭窄与各危险因素的 logistic 回归分析

将 SUA 四分位分别为 Q1 ($\text{SUA} \leq 286 \mu\text{mol/L}$)、Q2 ($286 \mu\text{mol/L} < \text{SUA} \leq 341 \mu\text{mol/L}$)、Q3 ($341 \mu\text{mol/L} < \text{SUA} \leq 405 \mu\text{mol/L}$) 和 Q4 ($\text{SUA} > 405 \mu\text{mol/L}$)。二

元 logistic 单因素回归分析(Model 1)显示,随 SUA 水平增加,患者冠状动脉血管重度狭窄风险显著增加,Q2、Q3 和 Q4 分层的冠状动脉重度狭窄风险是 Q1 分层患者的 1.674、2.008 和 2.233 倍($P < 0.001$);Model 2 为校正了年龄、性别、吸烟史和饮酒史的多因素 logistic 分析,其中 Q3 和 Q4 分层冠状动脉重度狭窄风险为 Q1 分层的 1.269 和 1.382 倍;Model 3 校正年龄、性别、吸烟史、饮酒史、体质指数(body mass index, BMI)、LDL-C、HDL-C、总胆固醇、甘油三酯、肌酐和血糖等因素后 Q3 和 Q4 分层分别为 Q1 分层患者冠状动脉重度狭窄风险的 1.267 和 1.372 倍(表 3)。

2.3 不同年龄段患者冠状动脉血管狭窄与 SUA 水平 ROC 曲线下面积分析

为了更好地体现 SUA 预测中青年 CHD 患者冠状动脉血管重度狭窄风险的准确性,将该类 CHD 患者根据年龄分为 4 层,分别为 20 ~ 35 岁,36 ~ 45 岁,46 ~ 55 岁,56 ~ 65 岁,如图 1(A ~ D)。其中在 20 ~ 35 岁中,SUA 水平对 CHD 患者冠状动脉重度狭窄的预测价值最好,如表 4 所示。

表 3 二元 logistic 回归分析冠状动脉狭窄程度与 SUA 四分位相关风险[OR(95%CI)]

不同模型	SUA 四分位			
	Q1	Q2	Q3	Q4
Model 1	Ref.	1.674(1.345~2.082)**	2.008(1.620~2.488)**	2.233(1.804~2.763)**
Model 2	Ref.	1.207(0.958~1.521)	1.269(1.006~1.602)*	1.382(1.093~1.747)*
Model 3	Ref.	1.186(0.940~1.497)	1.267(1.000~1.604)	1.372(1.076~1.749)*

注:Ref. 表示参照;**表示与参照相比, $P<0.001$; *表示与参照相比, $P<0.05$ 。

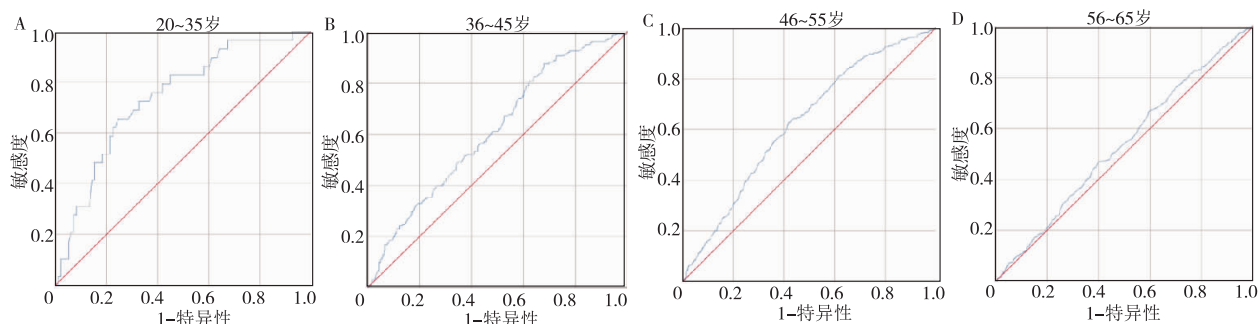


图 1 各年龄亚组中 SUA 对冠状动脉狭窄预测价值 ROC

表 4 各年龄亚组 ROC 曲线参数

年龄分层	AUC	95% CI	敏感性	特异性	临界值/($\mu\text{mol}\cdot\text{L}^{-1}$)	P 值
20~35 岁($n=127$)	0.741	0.641~0.840	65.5%	75.5%	422.5	<0.001
36~45 岁($n=544$)	0.614	0.564~0.664	87.6%	32.1%	309.5	<0.001
46~55 岁($n=1\,531$)	0.626	0.594~0.658	62.8%	58.0%	346.5	<0.001
56~65 岁($n=1\,755$)	0.534	0.504~0.564	66.9%	40.3%	306.5	0.028

注:AUC 为受试者工作特征曲线下面积。

2.4 35 岁以下亚组分析

以 $\text{SUA} \leq 422.5 \mu\text{mol/L}$ 及 $\text{SUA} > 422.5 \mu\text{mol/L}$ 对该年龄组患者进行分组,其基线资料分析如表 5 所示,两组只有肌酐水平和冠状动脉重度狭窄之间存在显著差异。二元 logistic 单因素分析(Model 1)显示,与 $\text{SUA} \leq 422.5 \mu\text{mol/L}$ 相比, $\text{SUA} > 422.5 \mu\text{mol/L}$ 的患者冠状动脉重度狭窄风险增加 4.8 倍;Model 2

校正年龄、吸烟史和饮酒史后,相比 $\text{SUA} \leq 422.5 \mu\text{mol/L}$, $\text{SUA} > 422.5 \mu\text{mol/L}$ 冠状动脉重度狭窄风险为 5.035 倍;Model 3 在 Model 2 的基础上继续校正 LDL-C、HDL-C、总胆固醇、甘油三酯、肌酐及空腹血糖、BMI 等混杂因素, $\text{SUA} > 422.5 \mu\text{mol/L}$ 为 $\text{SUA} \leq 422.5 \mu\text{mol/L}$ 冠状动脉重度狭窄风险 5.8 倍(表 6)。

表 5 35 岁以下患者的基线资料分析

变量	$\text{SUA} \leq 422.5 \mu\text{mol/L}$	$\text{SUA} > 422.5 \mu\text{mol/L}$	P 值
SUA/($\mu\text{mol}\cdot\text{L}^{-1}$)	338(304~374)	455(438~500)	<0.001
年龄/岁	32(30~34)	33(31~34)	0.259
性别[n(%)]			0.052
男性	67(79.8%)	40(93.0%)	
女性	17(20.2%)	3(7.0%)	
BMI/($\text{kg}\cdot\text{m}^{-2}$)	25.585(23.843~28.060)	26.530(24.130~30.200)	0.286
LDL-C/($\text{mmol}\cdot\text{L}^{-1}$)	1.600(1.310~1.870)	1.570(1.270~1.840)	0.718
HDL-C/($\text{mmol}\cdot\text{L}^{-1}$)	1.300(1.008~1.668)	1.390(0.990~1.650)	0.955
总胆固醇/($\text{mmol}\cdot\text{L}^{-1}$)	5.700(4.040~8.550)	6.550(4.710~8.210)	0.439
甘油三酯/($\text{mmol}\cdot\text{L}^{-1}$)	3.885(2.115~6.195)	5.600(2.800~6.710)	0.132
肌酐/($\mu\text{mol}\cdot\text{L}^{-1}$)	70(61~81)	76(68~84)	0.010
空腹血糖/($\text{mmol}\cdot\text{L}^{-1}$)	4.530(3.800~5.193)	4.760(3.980~5.620)	0.382
肌钙蛋白 I/($\text{ng}\cdot\text{mL}^{-1}$)	0.006(0.006~3.472)	0.063(0.006~10.695)	0.119
冠状动脉重度狭窄[n(%)]	10(11.9%)	19(44.2%)	<0.001
吸烟史[n(%)]	32(38.1%)	25(58.1%)	0.095
饮酒史[n(%)]	15(17.9%)	10(23.3%)	0.408

表 6 20~35 岁 CHD 患者与冠状动脉血管狭窄程度二元 logistic 回归分析

不同模型	SUA 分层		P 值
	SUA ≤ 422.5 μmol/L	SUA > 422.5 μmol/L OR(95% CI)	
Model 1	Ref.	5.858(2.397 ~ 14.315)	<0.001
Model 2	Ref.	5.035(1.923 ~ 13.185)	0.001
Model 3	Ref.	5.800(2.020 ~ 16.653)	0.001

注:Ref. 表示参照。

3 讨论

尿酸是人体内嘌呤代谢的终产物,既往研究发现高尿酸血症与高血压、糖尿病和代谢综合征等多种疾病密切相关^[11,21],但由于 SUA 与其他常规心血管危险因素(如吸烟、饮酒、肥胖、绝经状态和利尿剂应用等)之间有很强的相关性以及 SUA 本身的抗氧化能力,使得 SUA 与心血管疾病之间的关系错综复杂。本研究为了更好地探究 SUA 水平在中青年 CHD 患者中的影响,选用了 65 岁及以下中青年 CHD 患者(排除高血压、糖尿病、心力衰竭和痛风等影响 SUA 水平的疾病)人群,探讨该年龄段 CHD 人群 SUA 水平与冠状动脉狭窄程度间关系。本研究主要得出以下几点结论:(1)研究纳入 20~65 岁人群并排除了多种可能影响 SUA 水平的疾病因素后,发现 SUA 与入院后冠状动脉重度狭窄之间显著相关;(2)当对年龄进行分层后,在 20~35 岁 CHD 人群中,SUA 水平增高可能对重度冠状动脉狭窄具有较高预测价值,且 SUA > 422.5 μmol/L 的冠状动脉重度狭窄风险是 SUA ≤ 422.5 μmol/L 的 5.8 倍。

尽管目前 SUA 参与 CHD 的发病机制未完全阐明,但越来越多的人群流行病学研究发现 SUA 是 CHD 的独立危险因素^[22-24],高尿酸血症可能引起 CHD 患者的全因死亡率、心血管疾病死亡率和心源性猝死率显著升高^[25-28]。Kleber 等^[25]的研究发现 SUA 水平每增加 1 mg/dL,心血管疾病死亡风险增加 77% ($HR = 1.77, 95\% CI 1.12 \sim 2.81$),心源性猝死风险增加 1.4 倍 ($HR = 2.41, 95\% CI 1.16 \sim 5.00$)。此外,高尿酸血症还可能影响 CHD 患者 PCI 或冠状动脉搭桥术后预后及不良事件发生率。Lim 等^[29]对台湾地区的 PCI 术后患者进行随访发现高尿酸水平组 [$(7.20 \pm 2.39) \text{ mg/dL}$] 心血管疾病死亡率增加 6.45 倍 ($HR = 6.45, 95\% CI 2.52 \sim 16.55$);Shi 等^[30]研究认为冠状动脉搭桥术后高尿酸血症患者较 SUA 正常患者预后差,心血管不良事件发生风险增加 70% ($HR = 1.70, P = 0.01$),死亡率增加 1.4 倍 ($HR = 2.42, P = 0.004$)。Lin 等^[31]选取了 8 047 例痛风患者进行别嘌醇 ($HR = 0.28, 95\% CI 0.12 \sim 0.63, P < 0.05$)、苯马溴隆 ($HR = 0.46, 95\% CI 0.34 \sim 0.60, P < 0.001$) 等降尿酸治疗后

发现较高剂量降尿酸药物可以显著降低 CHD 风险,这可能与降尿酸治疗抑制黄嘌呤氧化酶、改善内皮功能和减少氧化应激反应等有关^[32]。

虽然 CHD 的流行病学数据大多来自老年人(> 65 岁),但其发病率在中国中青年人群中迅速增长^[3,33]。已知有各种危险因素与冠状动脉疾病的发病和发展有关。然而,在不同年龄段的人中,它们的贡献各不相同^[34-35]。随着 SUA 在 CHD 中的研究逐渐增多,SUA 是否在不同年龄段 CHD 发展中发挥独立因果作用的争论越来越多。最近几项关于 SUA 与中青年 CHD 的关系研究提供了相互矛盾的结果。在一项早发型 CHD(Early-onset CAD, EOCAD),年龄 < 45 岁的患者研究中发现,SUA 水平与血压、血脂显著相关,较高的 SUA 水平可能在心脏功能障碍和 EOCAD 的严重程度中起到重要作用^[27]。Zand 等^[36]的研究仅涉及 245 例 EOCAD 患者和 228 例正常冠状动脉受试者,他们发现 SUA 与 EOCAD 的存在显著相关,但它不是 EOCAD 的独立危险因素。Tian 等^[37]在研究中指出 EOCAD 组 SUA 水平显著高于对照组并且是 EOCAD 的独立危险因素 ($OR = 1.100, 95\% CI 1.022 \sim 1.185$),且 3 支血管病变的早发性心肌梗死患者的 SUA 水平高于 1 支或 2 支血管病变的患者。并且 EOCAD 高尿酸血症患者的 Gensini 评分高于无高尿酸血症的患者,表明 SUA 水平与 EOCAD 的存在和严重程度相关,这说明 SUA 可能参与 EOCAD 的进展。在这项回顾性研究中,评估了 3 957 例 65 岁及以下 CHD 患者中 SUA 与冠状动脉狭窄程度之间的关系,并检测出了阳性结果,通过二元 logistics 回归分析清楚地表明,随着 SUA 水平的升高,重度冠状动脉狭窄的发生风险显著增高。

目前对于高尿酸血症与 CHD 发生及其不良预后的机制有以下理论及假说:(1)当尿酸进入内皮细胞及平滑肌细胞或经细胞内嘌呤代谢产生时,尿酸从抗氧化剂转化为氧化增强剂,且对内皮细胞的氧化应激损伤大于细胞外抗氧化作用^[38]。(2)尿酸晶体通过促进趋化因子如单核细胞趋化蛋白-1、炎症因子如白介素-1、白介素-6 等的释放介导炎症反应,或促进缩血管因子如内皮素-1、血管紧张素-2 等释放,此外缺血损

伤的细胞释放尿酸激活免疫系统如树突状细胞等引起局部炎症反应^[39],从而介导冠状动脉病变。(3)尿酸可以通过增加精氨酸酶活性、抑制一氧化氮合成酶磷酸化从而影响一氧化氮生物利用度,影响冠状动脉舒缩及内皮细胞功能,且血尿酸可促进肾素-血管紧张素-醛固酮系统,介导血管平滑肌细胞增生^[39-41]。

另外,本研究是单中心回顾性研究,研究结果基于横断面数据,并且仅在首次入院时测量了 SUA,不能肯定地推断出 SUA 与冠状动脉狭窄程度发展之间的时间关联,因此以上研究结论还需要在多中心、前瞻性、随机对照研究中进行验证。

综上所述,研究发现 SUA 与中青年 CHD 患者重度冠状动脉狭窄显著相关,特别是在 20~35 岁 CHD 人群中,尿酸水平增高可能与重度冠状动脉狭窄风险具有更高相关性及预测性。这些发现可能有助于了解中青年 CHD 患者的发病机制和预测其进展,并可能有助于进一步预防该疾病。

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综上所述,SLE-PH 患者 ABCG1 和 GALNT2 甲基化构成比较高且 ABCG1 甲基化可能会影响 SLE 患者预后,NYHA 分级(Ⅲ~Ⅳ)是 SLE-PH 患者不良预后的危险因素。临床可增加 DNA 甲基化转移酶抑制剂治疗以逆转 ABCG1 和 GALNT2 表达水平,注重患者心功能恢复救治,改善心脏的相应调节功能,以延长患者生存时间。

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