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·临床研究·

血清尿酸水平与冠心病的相关性研究 *

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摘要 目的:众多关于血清尿酸水平与冠心病发展预后的相关性研究结果不一。本研究旨在通过对上海市第一人民医院入院患者的临床资料分析,研究血清尿酸水平与冠心病之间关系。**方法:**选择 2008 年 7 月至 2009 年 4 月上海地区、汉族就诊于我院的患者(123 例),按入选排除标准,将入院患者分为冠心病组和对照组,分析尿酸水平与冠心病的关系。**结果:**男性(81.4% vs 51.6%)、吸烟 (49.2% vs 21.9 %)、血清尿酸水平升高 (6.10± 1.2 mg/dl vs 5.37± 1.5 mg/dl) 为冠心病的危险因素，统计值分别为 0.02,0.02,0.005。血尿酸水平升高与血管病变严重程度成正相关,除单支血管病变外,双支血管病变患者尿酸水平为(6.11± 1.07) mg/dl,对照组为(5.37± 1.55) mg/dl,P< 0.05,三支病变患者尿酸水平为(6.84± 1.29) mg/dl,P< 0.05。**结论:**血清尿酸水平升高与冠心病的发生、及病变严重程度密切相关。对冠心病患者的预防和治疗中,应重视对尿酸水平的监测。尿酸水平能否作为冠心病患者预后、转归的预测因子以及降低尿酸水平的治疗能否给冠心病患者带来收益有待进一步的研究。

关键词:血尿酸;冠心病;危险因素

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Correlation of serum uric acid level with coronary artery disease*

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ABSTRACT Objective: There is discrepancy in the results on the relationship between the level of serum uric acid and coronary artery disease. The present study was to analyze the clinical data of inpatients with coronary artery disease and explore the relationship between the level of serum uric acid and coronary artery disease. **Methods:** The study enrolled 123 participants who were admitted to Shanghai First People's Hospital from July, 2008 to April, 2009. These patients were enrolled as coronary artery disease group and control group. Clinical data were analyzed. **Results:** Male (81.4% vs 51.6%), smoking (49.2% vs 21.9 %), elevated serum uric acid level (6.10± 1.2 mg/dl vs 5.37± 1.5 mg/dl) were associated with coronary artery (P = 0.02, 0.02, 0.005, respectively). Elevated serum uric acid level was positively correlated to the severity of coronary artery disease. Serum uric acid level in patients with two-vessel disease (6.11± 1.07 mg/dl) and that in patients with three-vessel disease were significantly higher than that in control group(6.84± 1.29 mg/dl, P<0.05). **Conclusions:** Elevated serum uric acid level is associated with the prevalence as well as severity of coronary artery disease. Emphasis should also be placed on the evolving prevalence of hyperuricemia. More studies are therefore warranted to determine the association between hyperuricemia and cardiovascular outcomes, and the potential value of specific urate-lowering treatment on cardiovascular disease.

Key words: Uric acid; Coronary artery disease; Risk factors

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前言

尿酸(uric acid,UA)是人体外源性和内源性嘌呤代谢的终产物。血清尿酸(serum uric acid,SUA)水平升高与体内核酸代谢异常和肾脏排泄减少有关。国际上将高尿酸血症(hyperuricemia,HUA) 的诊断标准定义男性 UA＞420 μmol/L(7 mg/dl),女性 UA＞357 μmol/L(6 mg/dl)。近年来,随着人们生活水平的提高和饮食结构的改变,HUA 的发病率有明显上升趋势。在过去的几十年里 HUA 与机体代谢功能紊乱有关的观点已被大家所公认。很多前瞻性队列研究发现,血清尿酸水平的升高与心血管疾病（cardiovascular disease,CVD）如高血压(hypertension,HBP)[1]、冠心病(coronary artery disease,CAD)[2]、

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充血性心力衰竭(congestive heart failure,CHF)[3]等的发生和发展密切相关,但可引起尿酸水平升高的因素如肥胖、高血压、高血糖、高血脂、胰岛素抵抗等也是心血管疾病发病的传统致病因素。因此 HUA 与 HBP、CAD、CHF 等心血管疾病具体关系研究结论不一[4]。近 20 年来有很多大规模前瞻性临床研究证实 HUA 是上述心血管疾病发生的独立的危险因素[5,6],并且血尿酸水平越高,发生冠心病的风险越大[7]。

最早关于人群中血清尿酸水平与心血管疾病转归的关系的研究是 Framingham 心脏研究[8,9],遗憾的是在其中两个观察组未得到一致的结论。此外,美国第一次全国健康与营养调查(the First National Heath And Nutrition Examination Survey, NHANESⅠ)随访发现高尿酸血症患者每年与心血管疾病有关的死亡增加 2 倍,在没有多个危险因素或代谢综合征的低危人群,尿酸仍是心血管病相关死亡的独立预测因素[10,11]。但有学者指出,NHANESⅠ研究也没有考虑血肌酐和血糖水平给试验结果带来的可能影响。可见,要想确立 HUA 与 CVD 的关系需要分析和调整很多协变量。本研究选取了 2008 年 7 月至 2009 年 4 月于上海市第一人民医院心内科住院治疗的患者共 123 例,分为冠心病组(59 例)和非冠心病组(64 例)。在考虑并调整了性别、年龄、血脂、血肌酐和血糖水平等多项变量因素的影响后,比较两组之间的血尿酸水平,分析尿酸水平的高低与冠心病的发病率之间的关系,以及尿酸水平的高低与冠状动脉病变严重程度的相关性。

1 资料和方法

1.1 资料

选择 2008 年 7 月至 2009 年 4 月于上海市第一人民医院心内科住院的患者。

对照组入选标准:①年龄在 30~80 岁;②心功能正常,NYHA 分级=Ⅰ级,LVEF>50%;③冠脉造影检查结果证实冠脉血管狭窄≤ 20%;④无器质性心脏病,如风心病、先天性心脏病。冠心病组入选标准:①年龄在 30~80 岁;②无心肌梗死的患者:冠状动脉造影结果至少一个主要分支(左前降支、左回旋支、右冠状动脉)狭窄程度>50%;或陈旧性心肌梗死患者;或急性心肌梗死患者:心肌梗死后 1 周 ~3 个月内;③出院时超声检查左室射血分数 LVEF≥ 50%(Simpson 法);④无器质性心脏病,如风心病、先天性心脏病。

剔除标准:①继发性高血压、痛风、甲状腺疾病、消化道溃疡、肺部疾病、血液系统疾史;②近期使用过噻嗪类利尿剂等药物;③血清肌酐>265 umol/L(≥ 3 mg/dl),谷草转氨酶>160 IU/L 或谷丙转氨酶>160 IU/L;④不稳定的颅脑病变;⑤恶性肿瘤;⑥认知功能障碍、痴呆患者,严重精神病患者;⑦其他严重未控制的各系统疾病;⑧准备或已经妊娠的女性患者、哺乳期妇女;⑨患者有明显的原因不能理解或配合完成所有随访检查者;⑩已经参加其他研究(仅指所参加项目不允许参加其他研究)者,不能或不愿意签署知情同意书的患者。

1.2 方法

所有患者均在我院接受过冠脉造影检查。根据照造影结果及心超检查,按入选和排除标准,将患者分为冠心病组和对照组。收集患者入院时的资料,包括性别、年龄、身高、体重、SUA、TCH、TG、LDL-C、HDL-C,以及糖尿病病史、吸烟史。

1.3 统计学处理

所有资料统计分析采用 SPSS10.0 统计软件,计量资料以 s 表示,分类变量用%表示。组间两两比较采用 t 检验,分类变量的比较采用卡方检验。多组间连续变量的比较采用方差分析。四格表资料采用卡方检验,以 $P<0.05$ 为用统计学差异。

2 结果

收集冠心病组 59 例,其中男性 48 例,女性 11 例;对照组 64 例,其中男性 33 例,女性 31 例。两组患者基线情况如表 1 所示。正常对照组和冠心病组基线资料比较可知,冠心病组男性及吸烟比率较对照组高,冠心病组 SUA 水平显著高于正常对照组((5.37+1.5) mg/dl vs (6.10+1.2) mg/dl,$P<0.01$)。男性、吸烟、血清尿酸水平升高为冠心病的危险因素。

表 1 冠心病组与对照组基线资料

Table 1 The baseline data of CAD and control groups

	control(n=64)	CAD(n=59)	Statitcs
Male(%)	33(51.6%)	48(81.4%)	x^2=0.02
Smoke(%)	14(21.9%)	29(49.2%)	x^2=0.02
DM(%)	12(18.8%)	11(18.6%)	x^2=0.98
Age(year,$\bar{x}\pm$ s)	59.9± 10.9	63.3± 10.8	P =0.88
BMI(kg/m2, $\bar{x}\pm$ s)	24.1± 3.1	24.3± 2.9	P =0.65
SUA(mg/dl,$\bar{x}\pm$ s)	5.37± 1.5	6.10± 1.2	P =0.005
SCr(umol/L,$\bar{x}\pm$ s)	65.9± 15.9	76.2± 28.5	P =0.17
GFR(ml/min/1.73m2,$\bar{x}\pm$ s)	96.7± 29.6	89.3± 30.5	P =0.17
Glu(mmol/L,$\bar{x}\pm$ s)	5.2± 1.0	5.4± 1.0	P =0.16
TC(mmol/L,$\bar{x}\pm$ s)	4.5± 1.0	4.3± 0.9	P =0.15
TG(mmol/L,$\bar{x}\pm$ s)	1.6± 1.1	1.5± 0.6	P =0.60
LDL-C(mmol/L,$\bar{x}\pm$ s)	2.7± 0.9	2.4± 0.8	P =0.08
HDL-C(mmol/L,$\bar{x}\pm$ s)	1.08± 0.25	1.01± 0.18	P =0.05

SUA 水平与冠状动脉病变严重程度的相关性分析结果如表 2 所示。结果显示冠状动脉病变支数越多,其 SUA 的水平越高，不同冠脉病变数目组间的 SUA 水平差异具有统计学意义(表 2)。考虑本研究入组的病人在年龄、糖尿病、体重指数、肌酐、血脂等因素无统计学差异,遂采用一元线性回归分析,结果显示:回归模型拟合度为 0.23,方差分析显示回归模型具有统计学意义(P< 0.01),该模型的标准化残差的直方图和正态 P-P 图具有正态分布趋势(图 1,图 2)。

表 2 血清尿酸水平与冠脉病变严重程度的相关性分析

Table 2 The correlation analysis of serum uric acid levels and the severity of coronary lesions

Group	Number	DM	SUA(mg/dl,$\bar{x}$± s)	p
control	64	12	5.37± 1.55	There was significant difference in the
Single-vessel	20	2	5.38± 0.96	SUA levels between the two groups in
Double-vessel	10	5	6.11± 1.07	control, double-vessel, and three-vessel
Three-vessel	19	4	6.84± 1.29	group (P < 0.05)

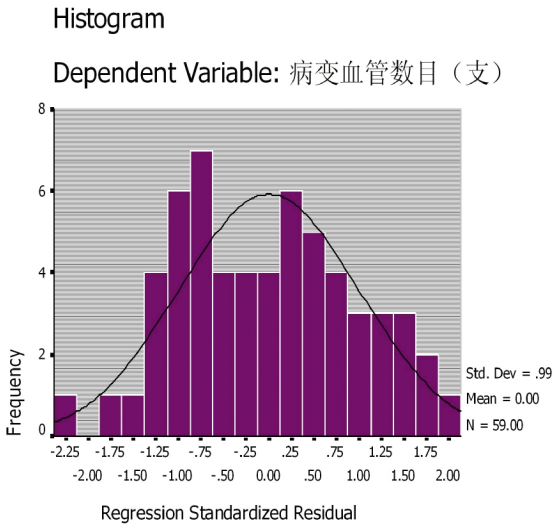

图 1 将 SUA 水平与冠状动脉血管病变支数进行回归分析的标准化残差直方图

Fig. 1 Standardized residuals histogram of SUA levels and the number of coronary artery vascular lesions by regression analysis

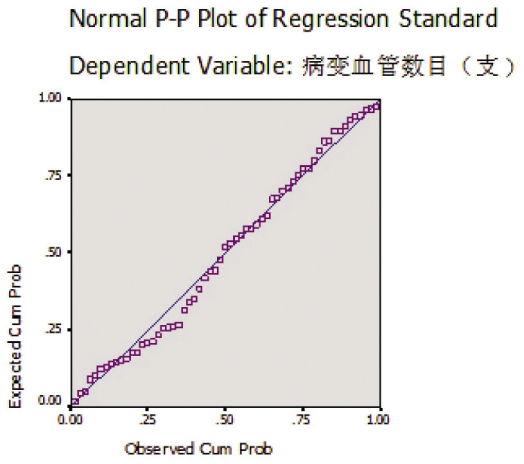

图 2 将 SUA 水平与冠状动脉血管病变支数进行回归分析的标准化残差正态 P-P 图

Fig. 2 Standardized residuals normal P - P of SUA levels and the number of coronary artery lesions by regression analysis

3 讨论

本研究证实 SUA 水平与冠心病的发生和进展密切相关,冠状动脉病变愈严重的患者,其 SUA 水平愈高,两者呈线性相关。多种研究显示 HUA 是全身及冠状动脉血管疾病独立的危险因素[12]。美国第三次全国健康与营养调查(the First National Heath and Nutrition Examination Survey,NHANES Ⅲ）入选了 16000 例患者，调查分析显示,SUA≥ 6 mg/L 可作为冠心病独立的危险因素[13]。尿酸每增加 1mg/dl,心血管疾病高危患者的死亡率就升高 39%[14]。

HUA 导致冠心病及不良预后的具体机制尚不明确，目前研究提示可能机制包括:(1)HUA 时，尿酸微结晶容易析出沉积于血管壁,直接造成血管内皮细胞损伤,引起内膜炎症反应。(2)尿酸盐作为炎症物质还可以激活血小板,促进血小板的粘附聚集和血小板血栓形成。(3)HUA 促进 LDL-C 氧化和脂质过氧化,使氧自由基产生增加,促进粥样板块的发生、发展等。(4)血尿酸浓度还与胰岛素敏感性血浆甘油三酯明显相关。

本研究显示 SUA 水平与冠心病及冠状动脉病变的严重程度显著相关。但单支病变组与正常对照组未发现显著统计学差异,分析考虑可能是正常对照组入组的糖尿病病人所占的比率较单支病变组高,在以后的研究中调整该因素,分析其对 SUA 水平的影响。有研究显示在非糖尿病、非高血压的急性冠脉综合症患者，血尿酸水平升高与病变血管数量增多明显相关,高尿酸为冠心病的一个独立危险因素[15]。本研究的结果提示早期对包括 SUA 在内的综合性因素进行干预可能有助于冠心病的防治。有研究显示使用别嘌呤醇降低尿酸水平可以降低高血压患者的血压水平 [16]，从而有助于改善高血压的预后。虽然降 SUA 治疗对冠心病及其预后的确切作用还需要更多的研究证实,但这无疑是冠心病治疗的一个新方向。

4 结论

本研究通过综合调整性别、年龄、血肌酐、血糖、血脂等多项影响因素后,分析结果显示:男性、吸烟与血清尿酸水平升高都是冠心病发生危险因素。并且血尿酸升高和血管病变严重程度成正相关,除单支病变外,双支和三支病变的血清尿酸水平均显著高于正常对照组。血尿酸水平越高,冠状动脉的病变越严重。由此,通过本研究可以得知血尿酸水平升高与冠心病的

发病率增高相关,与冠心病的严重程度相关。心力衰竭是心脏疾病进展的末期表现,在心脏病的末期阶段,尿酸是否也起着重要的作用?末期阶段的尿酸水平的高低,是否与患者的预后相关? 尿酸的水平的高低是否可以作为患者预警指标的一项,并由此判断患者的预后及转归?控制尿酸水平的治疗是否可以给冠心病患者带来收益? 在后期的研究中,我们将增加对心力衰竭患者的病例分析及预后随访观察,以更加明确尿酸水平在心血管疾病的发生、发展中所扮演的角色和所起到的作用,为冠心病的预防、诊治及康复指导提供依据。

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