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# 脑小血管病患者血清尿酸水平和步态障碍之间的相关性 *

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**摘要 目的：**探讨脑小血管病(Cerebral small vessel disease，CSVD)患者血清尿酸(Uric acid，UA)水平和步态障碍之间的相关性。**方法：**将我院自 2018 年 1 月至 2019 年 1 月收治的 CSVD 患者 172 例作为研究对象，根据患者血清尿酸水平分为研究组 87 例，对照组 85 例。收集和比较两组的临床资料，使用 Logistic 回归分析血清尿酸和 CSVD 患者脑室旁、深部白质高信号、步态障碍之间的相关性。**结果：**两组的年龄、性别、体质指数、血糖指标、血脂指标水平，合并高血压、糖尿病病史和吸烟情况比较差异无统计学意义($P$>0.05)。研究组血清尿酸水平、饮酒患者比例明显高于对照组($P$<0.05)，脑室旁高信号和深部白质高信号中重度比例均明显高于对照组($P$<0.05)；将步态障碍、脑室旁高信号与深部白质高信号作为影响因素带入相关分析，结果显示血清尿酸水平与步态障碍、脑室旁高信号与深部白质高信号比较存在正相关($P$<0.05)。**结论：**CSVD 患者血清高尿酸水平与脑室旁、深部白质高信号病变程度呈明显的正相关性，也是患者步态障碍的影响因素。

**关键词：**脑小血管病；血清尿酸；步态障碍；相关性

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# Correlation between Serum Uric Acid Level and Gait Disturbance in Patients with Cerebrovascular Disease*

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**ABSTRACT Objective:** To investigate the correlation between serum uric acid (UA) level and gait disorders in patients with cerebellar small vessel disease (CSVD). **Methods:** 172 patients with CSVD admitted to our hospital from January 2018 to January 2019 were divided into the study group (87 cases) and the control group (85 cases) according to the serum uric acid level. The clinical data of the two groups were collected and compared, and Logistic regression analysis of the correlation between paraventricular, deep white matter high signal and gait disorder in patients with serum uric acid and CSBD. **Results:** There was no significant difference in age, sex, body mass index, blood glucose index, blood lipid index, hypertension, diabetes mellitus and smoking status between the two groups ($P$>0.05). The serum uric acid level and the proportion of drinking patients in the study group was significantly higher than that in the control group ($P$<0.05). The high ratio of ventricular high signal and deep white matter high signal were significantly higher than the control group ($P$<0.05). The gait disorder, high paraventricular signal and deep white matter high signal were taken as the influencing factors. The results showed that there was a positive correlation between serum uric acid level and gait disorder, high paraventricular signal and deep white matter high signal ($P$<0.05). **Conclusion:** The serum hyperuricemia of CSVD patients is positively correlated with the severity of high signal lesions in paraventricular and deep white matter, which is also a risk factor for gait disorder.

**Key words:** Cerebrovascular disease; Serum uric acid; Gait disorder; Relevance

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## 前言

脑小血管病是指颅内小血管病变引起患者临床、认知、病理学表现的综合征，常累及颅内小动脉、微动脉、毛细血管和小静脉等，影像学检测会出现腔隙性梗死、脑微出血或脑白质疏松改变，临床上主要表现为认知功能逐渐下降、运动障碍、排尿障碍等症状，会对患者生活质量造成严重影响[1,2]。目前，关于 CSVD 的发病机制尚未完全明确，一般认为血清尿酸水平导致

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血管内皮损伤,或与急性缺血性脑卒中有关[3,4]。对于 CSVD 患者而言,CT 或 MRI 检查发现脑室旁或半卵圆中心高信号表现,因此脑白质高信号为其主要影像学特征,而高尿酸水平是 CSVD 患者发生重度脑白质高信号病变的独立危险因素。但 UA 水平是否影响 CSVD 患者步态障碍症状尚未阐明 [5,6]。为此,本研究将我院近一年来收治的 CSVD 患者作为研究对象,根据尿酸水平分组后使用 Logistic 回顾性分析 UA 水平和患者步态障碍之间的相关性,现报道如下。

## 1 资料与方法

### 1.1 一般资料

将我院自 2018 年 1 月至 2019 年 1 月收治的 CSVD 患者 172 例作为研究对象,根据患者血清尿酸水平(分组标准[7]为男性 UA≥ 428 μmoL/L,女性≥ 357 μmoL/L)分为研究组 87 例,对照组 85 例。研究组男 47 例,女 40 例,年龄 40~83 岁,平均年龄 61.81± 4.29 岁;对照组男 46 例,女 39 例,年龄 41~82 岁,平均年龄 61.67± 4.36 岁,两组一般资料比较差异无统计学意义($P$＞0.05)。

### 1.2 纳入与排除标准

所有患者均符合 2010 年国家颁布的关于脑卒中的诊断标准,经 MRI 诊断脑白质存在高密度阴影,颅内存在存在明显的腔隙性脑梗死病灶,磁敏感加权成像直径 2~5 mm 信号缺失区域。研究组患者为高尿酸浓度组[8,9]。

排除标准:将 MRI 禁忌症人群,存在严重大血管疾病或腔隙性脑梗死、微血管出血以外的脑出血史患者,老年痴呆者和其他原因导致的脑白质损害或影响运动和神经系统病变、存在关节损害和严重骨质疏松症患者排除。

所有患者均在知情同意的情况下上报医院伦理委员会,经批准后进行研究。

### 1.3 方法与观察指标

(1)分析两组的临床资料特点,选择两位神经内科主任分别对两组的总体认知水平进行评估和测定,同时建立良好的沟通桥梁,取得患者的信任。(2)步态障碍评定测量[10,11]:患者均通过 10 m 行走实验测量步长、步宽、步频和步速,起立行走实验观察每位对象的行走时间,使用步态量表对步态和平衡感进行分级积分,做好相关记录。(3)血清尿酸水平:空腹状态下采集患者肘静脉血 2 mL 置于含有 EDTA 的抗凝管中,3000 r/min 离心 10 min,使用上海可华生物试剂有限公司生产的试剂盒,按照比色法测定,使用强生 VITROS3600 全自动免疫分析仪测定 UA 水平,同时检测患者血脂、血糖、血压等生化指标的水平。(4)影像学观察。

### 1.4 统计学方法

使用 SPSS21.0 软件进行数据分析,计数资料以(%)表示,组间比较采用 $x^2$ 检验,计量资料以($\bar{x}$± $s$)表示,组间比较采用 t 检验,相关分析采用 Logistic 回归分析,以 $P$＜0.05 为差异有统计学意义。

## 2 结果

### 2.1 两组一般资料的比较

两组的年龄、性别、体质指数(Body Mass Index,BMI)、空腹血糖 (Fasting blood sugar,FBS)、糖化血红蛋白(Glycosylated hemoglobin,HbA1c)、总胆固醇(Total cholesterol,TC)、甘油三酯(Triglyceride)、高密度脂蛋白胆固醇 (High-density lipoprotein cholesterol,HDL-C)、低密度脂蛋白胆固醇(Low-density lipoprotein cholesterol,LDL-C)等生化指标水平,合并高血压、糖尿病病史和吸烟比较差异无统计学意义($P$＞0.05),但研究组的血清尿酸 (Serum uric acid,SUA) 水平、饮酒比例明显高于对照组($P$＜0.05),详见表 1。

表 1 两组一般资料的比较

Table 1 Comparison of the general information between two groups

| Index | Study group (87 cases) | Control group (85 cases) | t/$x^2$ | $P$ |
|---|---|---|---|---|
| Age (age) | 61.81± 4.29 | 61.67± 4.36 | 0.212 | 0.832 |
| Sex | | | | |
| male | 47(54.02) | 46(54.12) | 0.351 | 0.764 |
| female | 40(45.98) | 39(45.88) | | |
| BMI(kg/m$^2$) | 23.62± 2.14 | 23.45± 2.11 | 0.525 | 0.600 |
| SUA(umol/L) | 432.20± 62.81 | 287.28± 78.49 | 13.385 | ＜0.001 |
| FBS(mmol/L) | 5.62± 1.34 | 5.70± 1.32 | -0.394 | 0.694 |
| HbA1c(mmol/L) | 6.91± 4.12 | 6.67± 3.98 | 0.388 | 0.698 |
| TC(mmol/L) | 4.32± 0.94 | 4.28± 0.89 | 0.286 | 0.775 |
| Triglyceride(mmol/L) | 1.44± 0.65 | 1.39± 0.78 | 0.457 | 0.648 |
| LDL-C(mmol/L) | 3.16± 1.45 | 2.87± 1.38 | 1.343 | 0.181 |
| HDL-C(mmol/L) | 1.28± 0.70 | 1.30± 0.74 | 0.729 | 0.467 |
| Hypertension[n(%)] | 51(58.62) | 48(56.47) | 0.741 | 0.438 |
| Diabetes[n(%)] | 18(20.69) | 17(20.00) | 1.528 | 0.167 |
| Drinking [n(%)] | 52(59.77) | 35(41.18) | 1.912 | 0.046 |
| Smoking[n(%)] | 41(47.13) | 38(44.71) | 0.297 | 0.819 |

### 2.2 不同尿酸水平患者脑部白质高信号程度比例

研究组的脑室旁高信号和深部白质高信号中重度比例均明显高于对照组($P<0.05$),详见表 2。

表 2 不同尿酸水平患者脑部白质高信号程度比例

Table 2 Comparison of the Proportion of white matter high signal intensity between patients with different uric acid levels

| Groups | Cases | Paraventricular hyperintensity | | Deep white matter hypersignal | |
|---|---|---|---|---|---|
| | | No or mild | Moderate to severe | No or mild | Moderate to severe |
| Study group | 87 | 29(33.33) | 58(66.67) | 34(39.08) | 53(60.92) |
| Control group | 85 | 45(52.94) | 40(47.06) | 44(51.76) | 41(48.24) |
| $x^2$ | - | 5.136 | | 4.354 | |
| $P$ | - | 0.013 | | 0.025 | |

### 2.3 血清尿酸水平与步态障碍的关系

研究组中步态障碍发生率 49(56.32%),显著低于对照组 65(80.00%,$P<0.05$)。

### 2.4 血清尿酸水平与步态障碍和脑部白质高信号相关性分析

将步态障碍、脑室旁高信号与深部白质高信号作为影响因素带入相关分析,结果显示血清尿酸水平与步态障碍、脑室旁高信号与深部白质高信号比较存在正相关($P<0.05$),详见表3。

表 3 两组不同血清尿酸水平与步态障碍和脑部白质高信号之间的关系

Table 3 Relationship between different levels of serum uric acid levels and gait disorders and high white matter in the brain

| Index | r | $P$ |
|---|---|---|
| Gait disorder | 0.321 | 0.02 |
| Periventricular hyperintensity | 0.238 | 0.03 |
| Deep white matter high signal | 0.416 | 0.00 |

## 3 讨论

脑小血管病患者能够引起的临床、认知和影像学等一系列改变的综合征[12-14],是造成患者出现血管性轻度认知障碍的重要原因,若病情进一步发展会转化为血管性痴呆[15-17]。步态障碍是人群运动障碍中最常见的类型之一,对患者生活能力、疾病预后均会产生不良影响,尤其对于老年患者而言,腔隙性脑梗死和白质损害与其步态障碍有明显的相关性[18-20]。

尿酸是体内嘌呤代谢的最终产物,高尿酸水平会通过对血管内皮炎症反应和氧化应激发挥促进作用,造成血管内皮功能紊乱和白质损伤,从而对患者认知功能产生影响[21,22]。本研究根据男性 UA≥ 428 μmol/L,女性≥ 357 μmol/L 的标准将我院收治的脑小血管病患者分为高尿酸症的研究组和低尿酸症的对照组,研究组的 SUA 水平、饮酒比例明显高于对照组[23,24],脑室旁高信号和深部白质高信号中重度比例均明显高于对照组,提示血清尿酸水平和脑室旁高信号与深部白质高信号呈正相关[25,26]。有资料显示随着血清尿酸水平增高,患者脑白质病变程度逐渐增加。如果患者血清尿酸水较高,其脑萎缩和认知功减退越明显[27,28]。本研究将进一步将步态障碍、脑室旁高信号与深部白质高信号作为影响因素带入相关分析,结果显示血清尿酸水平与步态障碍、脑室旁高信号与深部白质高信号比较存在正相关,血清高尿酸水平作为独立危险因素影响着患者步态表现[29,30]。

综上所述,CSVD 患者血清高尿酸水平与脑室旁、深部白质高信号病变程度呈明显的正相关性,也是患者步态障碍的影响因素,随着尿酸水平越高,患者的步态障碍越为严重。

## 参 考 文 献(References)

[1] Nagai K, Koshiba H, Shibata S, et al. Relationship of Serum Carnitine Level with Falls and Gait Disturbance in the Elderly [J]. J Frailty Aging, 2017, 6(4): 178-182

[2] Ou R, Cao, Bei, Wei, Qianqian, et al. Serum uric acid levels and freezing of gait in Parkinson's disease[J]. Neurol Sci, 2017, 38(6): 955-960

[3] Allali G, Kern I, Laidet M, et al. Parkinsonism is a Phenotypical Signature of Amyloidopathy in Patients with Gait Disorders [J]. J Alzheimers Dis, 2018, 63(4): 1373-1381

[4] Essex MN, Hopps M, Bienen EJ, et al. Evaluation of the Relationship Between Serum Uric Acid Levels and Cardiovascular Events in Patients with Gout: A Retrospective Analysis Using Electronic Medical Record Data[J]. J Clin Rheumatol, 2017, 23(3): 160-166

[5] Jeong HY, Cho HJ, Kim SH, et al. Association of serum uric acid level with coronary artery stenosis severity in Korean end-stage renal disease patients[J]. Kidney Res Clin Pract, 2017, 36(3): 282-289

[6] Kawase S, Kowa H, Suto Y, et al. Association between Serum Uric Acid Level and Activity of Daily Living in Japanese Patients with Ischemic Stroke[J]. J Stroke Cerebrovasc Dis, 2017, 26(9): 1960-196

[7] Tanaka Y, Nagoshi T, Kawai M, et al. Close linkage between serum uric acid and cardiac dysfunction in patients with ischemic heart disease according to covariance structure analysis [J]. Sci Reports, 2017, 7(1): 2519-2529

[8] Adnan K, Hassan SM, Sarbiland K, et al. Serum Uric Acid level in the severity of Congestive Heart Failure (CHF)[J]. Pak J Med Sci, 2017, 33(2): 330-334

[9] Evans NR, Tarkin JM, Buscombe JR, et al. PET imaging of the neu-

rovascular interface in cerebrovascular disease [J]. Nat Rev Neurol, 2017, 13(11): 676-688

[10] Harrigan MR, Deveikis JP. Handbook of Cerebrovascular Disease and Neurointerventional Technique[M]. 2009

[11] Wang J, Chen Y, Liu B, et al. Systematic Investigation of the Erigeron breviscapus Mechanism for Treating Cerebrovascular Disease[J]. J Ethnopharmacol, 2018, 224(23): 429-440

[12] Santos, Cláudia Y, Snyder PJ, et al. Pathophysiologic relationship between Alzheimer\"s disease, cerebrovascular disease, and cardiovascular risk: A review and synthesis [J]. Alzheimers Dement (Amst). 2017, 7(10): 69-87

[13] Goetzl E, Schwartz J, Mustapic M, et al. Altered cargo proteins of human plasma endothelial cell-derived exosomes in atherosclerotic cerebrovascular disease[J]. FASEB J, 2017, 31(8): 23-26

[14] Goins RT, Schure MB, Jensen PN, et al. Lower body functioning and correlates among older American Indians: The Cerebrovascular Disease and Its Consequences in American Indians Study [J]. Bmc Geriatrics, 2018, 18(1): 6-17

[15] Smith EE, Saposnik G, Biessels GJ, et al. Prevention of Stroke in Patients With Silent Cerebrovascular Disease: A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association[J]. Stroke, 2017, 48(2): e44-e71

[16] Amato M, Mansi L, Val M. Imaging of Cerebrovascular Disease. A Practical Guide [J]. Eur J Nucl Med Mol Imaging, 2018, 45 (4): 674-674

[17] Victorio-Meza H, Manuel Mejía-Lavalle, Alicia Martínez Rebollar, et al. Searching for Cerebrovascular Disease Optimal Treatment Recommendations Applying Partially Observable Markov Decision Processes [J]. Intern J Pattern Recognit Artif Intell, 2018, 32(01): e11

[18] Peker, Yüksel, Strollo PJ. CPAP did not reduce cardiovascular events in patients with coronary or cerebrovascular disease and moderate to severe obstructive sleep apnoea [J]. Evid Based Med, 2017, 22 (2): 67-68

[19] He Z, Tang Y, Qin C. Increased circulating leukocyte-derived microparticles in ischemic cerebrovascular disease [J]. Thromb Res, 2017, 154(23): 19-25

[20] Smith EE, Saposnik G, Biessels GJ, et al. Prevention of Stroke in Patients with Silent Cerebrovascular Disease: A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association[J]. Stroke, 2017, 48(2): e44

[21] Backhouse EV, McHutchison, Caroline A, Cvoro, Vera, et al. Early life risk factors for cerebrovascular disease [J]. Neurology, 2017, 88 (10): 976-984

[22] Boltze J, Nitzsche F, Jolkkonen J, et al. Concise review: Increasing the validity of cerebrovascular disease models and experimental methods for translational stem cell research [J]. Stem Cells, 2017, 35 (5): 1141-1153

[23] Biffi A, Scotti L, Corrao G. Use of antidepressants and the risk of cardiovascular and cerebrovascular disease: a meta-analysis of observational studies[J]. Eur J Clin Pharmacol, 2017, 73(4): 1-11

[24] Schneider ALC, Selvin E, Sharrett AR, et al. Diabetes, Prediabetes, and Brain Volumes and Subclinical Cerebrovascular Disease on MRI: The Atherosclerosis Risk in Communities Neurocognitive Study (ARIC-NCS)[J]. Diabetes Care, 2017, 40(11): 1514-1521

[25] Zuo FT, Liu H, Wu HJ, et al. The effectiveness and safety of dual antiplatelet therapy in ischemic cerebrovascular disease with intracranial and extracranial arteriostenosis in Chinese patients: A randomized and controlled trail[J]. Medicine, 2017, 96(1): e5497

[26] Tocci G, Cicero AF, Massimo Salvetti, et al. Attitudes and preferences for the clinical management of hypertension and hypertension-related cerebrovascular disease in the general practice: results of the Italian hypertension and brain survey[J]. Clin Hypertens, 2017, 23 (1): 10-20

[27] Crawford KM, Gallegofabrega C, Kourkoulis C, et al. Cerebrovascular Disease Knowledge Portal: An Open-Access Data Resource to Accelerate Genomic Discoveries in Stroke [J]. Stroke, 2018, 49 (2): 470-475

[28] Perez-Lazaro C, Santos-Lasaosa S, Velazquez-Benito A, et al.Knowledge of cerebrovascular disease in the population of Zaragoza[J]. Rev Neurol, 2017, 64(1): 17-26

[29] Chong J, Liu S, Loke YM, et al. Influence of cerebrovascular disease on brain networks in prodromal and clinical Alzheimer's disease[J]. Brain, 2017, 140(11): 3012-3022

[30] Wright CB, Dong C, Perez EJ, et al. Subclinical Cerebrovascular Disease Increases the Risk of Incident Stroke and Mortality: The Northern Manhattan Study[J]. J Am Heart Assoc, 2017, 6(9): e004069