·临床研究·

血清尿酸对急性冠脉综合征患者治疗后6个月内再入院的预测价值

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【摘 要】 目的 探讨血清尿酸(SUA)对急性冠脉综合征(ACS)患者治疗后6个月内再入院的预测价值。**方法** 选取2016年1月至2019年3月于中国人民解放军总医院海南医院心血管内科住院治疗的ACS患者为研究对象。采用单因素分析及二元logistic回归分析探究SUA对ACS患者治疗后6个月内再入院的相关危险因素。通过受试者工作特征(ROC)曲线分析SUA对于再入院的预测价值。采用SAS9.4和R4.0.3软件进行数据分析。根据数据类型,组间比较分别采用t检验、Mann-Whitney U检验、χ^2检验及Bonferroni检验。**结果** 共纳入462例患者,再入院组47例,非再入院组415例。单因素分析结果显示,2组治疗方式比较,差异有统计学意义($P<0.05$);再入院组高血压、SUA、关节结石及住院期间不良事件发生情况均高于非再入院组,差异均有统计学意义[34例(72.34%)和231例(55.66%),(394.77±106.29)和(346.17±91.58)μmol/L,13例(27.66%)和18例(4.34%),12例(14.46%)和16例(3.86%);均$P<0.05$];再入院组肾小球滤过率和他汀类药物使用人数低于非再入院组,差异均有统计学意义[81.04(72.01,106.02)和92.98(78.76,106.62) ml/(min·1.73 m^2),36例(76.60%)和372例(89.64%);均$P<0.05$]。多因素分析结果显示,SUA(OR=1.004,95%CI 1.001~1.006)、治疗方式(OR=5.027,95%CI 2.855~8.853)、住院期间不良事件(OR=0.144,95%CI 0.050~0.410)与出院后6个月再住院相关($P<0.05$)。且随血清尿酸水平的升高,ACS患者再入院比例升高。SUA对出院后6个月内再入院事件的曲线下面积为0.649。**结论** SUA水平升高会增加ACS患者治疗后6个月内再入院的风险,并对再入院的风险具有一定的预测价值。

【关键词】 血清尿酸;急性冠脉综合征;再入院;危险因素

【中图分类号】 R541.4 **【文献标志码】** A **【DOI】** 10.11915/j.issn.1671-5403.2022.09.146

Predictive value of serum uric acid on readmission of acute coronary syndrome patients within 6 months after treatment

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【Abstract】 Objective To investigate the association of serum uric acid (SUA) with readmission within 6 months after treatment in patients with acute coronary syndrome (ACS), and to investigate the predictive value of SUA for readmission within 6 months. **Methods** A retrospective cohort trial was carried out on the ACS patients hospitalized in Department of Cardiology of Chinese PLA General Hospital Hainan Hospital from January 2016 to March 2019. Univariate and binary logistic regression analyses were used to explore the related risk factors of readmission within 6 months after treatment. Receiver operating characteristic (ROC) curve was drawn to analyze the predictive performance of SUA for readmission. SAS9.4 and R4.0.3 were used for statistical analysis. Data comparison between two groups was perfomed using t test, Mann-Whitney U test, χ^2 test or Bonferroni test depending on data type. **Results** A total of 462 patients were included in this study, and 47 of them were finally assigned into the readmission group and 415 into the non-readmission group in 6 months after treatment. Univariate analysis showed statistical significance in treatment method between the 2 groups ($P<0.05$). The patients from the readmission group had obviously higher SUA level (394.77±106.29 *vs* 346.17±91.58 μmol/L), larger ratios of hypertension [34 (72.34%) *vs* 231 cases (55.66%)], arthrolithiasis [13 (27.66%) *vs* 18 cases (4.34%)], and higher incidence of adverse events during hospitalization [12 (14.46%) *vs* 16 cases (3.86%)], but lower estimated glomerular filtration rate [1.04 (72.01, 106.02) *vs* 92.98 (78.76, 106.62) ml/(min·1.73 m^2)] and proportion of statin use [36 (76.60%) *vs* 372 cases (89.64%)] when compared with those of the non-readmission group (all $P<0.05$). Multivariate analysis indicated that SUA level (OR=1.004, 95%CI 1.001-1.006), treatment method (OR=5.027, 95%CI 2.855-8.853) and

收稿日期:2022-06-19;**接受日期**:2022-07-22

基金项目:海南省科技计划(临床医学研究中心)项目(LCYX202106)

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adverse events during hospitalization (*OR* = 0.144, 95%*CI* 0.050–0.410) were closely associated with readmission within 6 months after discharge (all *P*<0.05). The higher the SUA level was, the higher proportion of readmission in the ACS patients, and the area under the ROC curve of SUA for readmission was 0.649. **Conclusion** Elevated SUA level increases the risk of readmission within 6 months after discharge in ACS patients and has predictive value for the risk.

【Key words】 serum uric acid; acute coronary syndrome; readmission; risk factors

This work was supported by the Project for Clinical Medical Research Center of Hainan Science and Technology Plan (LCYX202106).

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急性冠脉综合征(acute coronary syndrome, ACS)是一种常见而严重的心血管疾病,有较高的发病率和死亡率[1]。ACS 患者 30 d 再入院率为 11%~35%,1 年再入院率为 40%~60%[2,3]。再入院导致患者预后不良的同时,增加了其精神和经济负担,还导致医疗资源利用效率降低等不良后果[4]。在因 ACS 入院的患者中,血清尿酸(serum uric acid, SUA)与院内和长期的全因死亡率和心血管死亡率、更高的院内不良事件发生率[5,6]、以及更长的住院时间有关。Stamp 等[7]的研究表明痛风患者随 SUA 水平的增加因心力衰竭再次入院的风险增加。目前,国内缺乏探讨 SUA 水平是否与 ACS 治疗后再入院风险相关的研究。本研究旨在探讨 SUA 与 ACS 治疗后 6 个月内再入院的相关性,并研究 SUA 对 ACS 患者治疗后 6 个月再入院的预测价值。

1 对象与方法

1.1 研究对象

选取 2016 年 1 月至 2019 年 3 月在中国人民解放军总医院海南医院心血管内科住院的 571 例 ACS 患者为研究对象。纳入标准:(1)年龄≥18 岁,性别不限;(2)首次确诊为 ACS,经住院治疗后出院;(3)患者基线资料、实验室检查资料及影像检查资料完整;(4)患者再入院原因为发生心血管事件。排除标准:(1)患者有瓣膜性心脏病、心肌病及高血压性心脏病;(2)首次住院期间或之后死亡的患者。受试者对研究临床和随访数据采集签署知情同意书,本研究获得解放军总医院海南医院伦理委员会批准。

1.2 方法

1.2.1 资料收集 收集患者入院一般资料,临床特征和实验室指标。一般资料包括性别、年龄、身高、体质量、体质量指数(body mass index, BMI)及烟酒史;临床特征包括冠状动脉病变严重程度(Gensini 评分)、ACS 类型、病变血管数、治疗方式及是否有合并症等;实验室检查指标包括血常规、血脂、SUA、心脏功能指标和肾功能等。收集患者是否入住重症监护室及住院期间不良事件等情况。

1.2.2 结局事件和随访 结局事件为 ACS 患者经过治疗后 6 个月内发生再入院事件。通过电话和患者复查随访,随访终点为患者发生再入院事件或截止到 2019 年 9 月 12 日。

1.3 统计学处理

采用 SAS 9.4 和 R4.0.3 统计软件进行分析。符合正态分布的计量资料用均数±标准差($\bar{x}\pm s$)表示,采用独立样本 t 检验;非正态分布的计量资料,用中位数(四分位数间距)[$M(Q_1, Q_3)$]表示,采用 Mann-Whitney U 检验。计数资料用例数(百分率)表示,采用 χ^2 检验,多组间两两比较采用 Bonferroni 检验。采用二元 logistic 回归分析探究相关危险因素与再入院的关系。通过受试者工作特征(receiver operating characteristic, ROC)曲线分析 SUA 对于再入院的判断能力。*P*<0.05 为差异有统计学意义。

2 结 果

2.1 2 组患者基线资料比较

571 例患者中,重复收集患者 9 例,死亡患者 2 例,患有心肌病 8 例,因非心血管事件再入院患者 3 例,因数据缺失被删除患者 87 例(分别为缺失体质量数据 3 例、Gensini 评分 6 例、脑利钠肽 28 例、总胆固醇 12 例、左室射血分数 3 例、用药情况 28 例及肌酸激酶同工酶 7 例),最终共纳入患者 462 例。按照 6 个月内是否再次入院分为 2 组,再入院组患者 47 例(10.17%),非再入院组患者 415 例(89.83%)。

出院后 6 个月内,2 组间治疗方式、高血压、SUA、关节结石、肾小球滤过率(estimated glomerular filtration rate, eGFR)、住院期间是否有不良事件和他汀类药物比较,差异均有统计学意义(*P*<0.05);其他指标比较,差异均无统计学意义(表 1)。

2.2 ACS 患者 6 个月内再入院危险因素二元 logistic 回归分析

单因素分析筛选出治疗方式、高血压、他汀类药物、住院期间不良事件、SUA 及 eGFR 等纳入回归分析。二元 logistic 回归模型发现 SUA、治疗方式、住院期间不良事件与出院后 6 个月再住院相关(*P*<0.05;表 2)。

将研究人群根据 SUA 水平及是否痛风分组,分正常 SUA 组、高 SUA 未确诊痛风组和痛风组。3 组患者 6 个月再入院率,正常尿酸组为 7.92%(29/366),高尿酸未痛风组为 13.85%(9/65),高尿酸痛风组为 29.03%(9/31),3 组间两两比较差异均有统计学意义(均 *P*<0.05)。

表1 2组患者基线资料比较

Table 1 Baseline data comparision between two groups

Item	Total(n=462)	Non readmission group (n=415)	Readmission group (n=47)	χ^2/ t/ Z	P value
Male[n(%)]	348(75.32)	314(75.66)	34(72.34)	0.251	0.617
Age(years, $\bar{x}\pm s$)	64.22±10.03	63.94±9.82	65.63±10.98	−1.489	0.137
Height (cm, $\bar{x}\pm s$)	168.25±8.02	167.31±7.08	169.19±9.34	0.410	0.686
Body mass(kg, $\bar{x}\pm s$)	70.27±11.63	70.24±11.57	70.46±12.23	−0.120	0.902
Smoking[n(%)]	222(48.05)	203(48.92)	19(40.43)	1.219	0.270
Alcohol drinking[n(%)]	172(37.23)	158(38.07)	14(29.79)	1.240	0.265
Gensini score [points, $M(Q_1, Q_3)$]	41.49(21.00,68.00)	40.00(24.00,60.00)	45.00(28.00,68.00)	1.280	0.201
ACS type[n(%)]				4.895	0.086
NSTEMI	69(14.94)	61(14.70)	8(17.02)		
STEMI	121(26.19)	115(27.71)	6(12.77)		
Unstable angina	272(58.87)	239(57.59)	33(70.21)		
Number of diseased vessels[n(%)]				1.612	0.447
1	166(35.93)	153(36.87)	13(27.66)		
2	136(29.44)	121(29.16)	15(31.91)		
3	160(34.63)	141(33.98)	19(40.43)		
Treatment[n(%)]				18.343	<0.001
PCI	418(90.48)	388(93.49)	30(63.83)		
Others*	44(9.52)	27(6.51)	17(36.17)		
Diabetes millitus[n(%)]	160(34.63)	139(33.49)	21(44.68)	2.334	0.127
Hypertension[n(%)]	265(57.36)	231(55.66)	34(72.34)	4.801	0.028
Other complications#[n(%)]	316(68.40)	280(67.47)	36(76.60)	1.627	0.202
Serum uric acid(μmol/L, $\bar{x}\pm s$)	351.12±94.21	346.17±91.58	394.77±106.29	−3.390	<0.001
Arthrolithiasis [n(%)]	31(6.71)	18(4.34)	13(27.66)	22.092	<0.001
Total cholesterol[mmol/L, $M(Q_1, Q_3)$]	3.87±1.05	3.88±1.03	3.78±1.23	0.600	0.549
LDL-C[mmol/L, $M(Q_1, Q_3)$]	2.26(1.78,3.05)	2.29(1.79,3.06)	2.13(1.46,3.01)	−1.464	0.143
Brain natriuretic peptide[pg/ml, $M(Q_1, Q_3)$]	157.00(58.00,821.00)	147.00(59.00,776.00)	227.00(53.00,2360.00)	1.141	0.254
LVEF(%)	54.62±3.27	55.40±2.45	53.84±4.08	0.760	0.561
eGFR [ml/(min·1.73m^2), $M(Q_1, Q_3)$]	92.42(77.41,106.02)	92.98(78.76,106.62)	81.04(72.01,106.02)	−2.068	0.039
Admission to CCU[n(%)]	111(24.03)	103(24.82)	8(17.02)	1.406	0.236
Adverse event during hospitalization△[n(%)]	28(5.62)	16(3.86)	12(14.46)	19.387	<0.001
ACEI/ARB[n(%)]	97(21.00)	84(20.24)	13(27.66)	1.401	0.237
Statins using[n(%)]	408(88.31)	372(89.64)	36(76.60)	6.958	0.008

*Including thrombolytic therapy and drugs; #including cardiac arrest, acute renal injury, hemorrhage, cardiogenic shock, acute respiratory failure, *etc*; △including congestive heart failure, end-stage renal disease, peripheral vascular disease, *etc*. ACS: acute coronary syndrome; NSTEMI: non ST elevated myocardial infarction; STEMI: ST elevated myocardial infarction; PCI: percutaneous coronary intervention; LDL-C: low-density lipoprotein cholesterol; LVEF: left ventricular ejection fractions; eGFR: estimated glomerular filtration rate; CCU: coronary care unit; ACEI/ARB: angiotensin-converting enzyme inhibitors/angiotension Ⅱ receptor blockers.

表2 ACS患者6个月内再入院危险因素二元logistic回归分析

Table 2 Binary logistic regression model for risk factors of ACS patients in 6-month readmission

Item	B	SE	Wald χ^2	P value	OR	95%CI
Serum uric acid	0.004	0.001	7.260	0.007	1.004	1.001−1.006
PCI	1.615	0.289	31.284	0.000	5.027	2.855−8.853
Hypertension	−0.360	0.260	1.917	0.166	0.698	0.419−1.161
Adverse event during hospitalization	−1.940	0.534	13.174	0.000	0.144	0.050−0.410
Statins using	0.618	0.334	3.419	0.064	1.856	0.964−3.575
eGFR	−1.176	0.887	1.759	0.185	0.308	1.032−1.140

ACS: acute coronary syndrome; PCI: percutaneous coronary intervention; eGFR: estimated glomerular filtration rate.

2.3 SUA对ACS患者治疗后6个月内再入院的预测价值

ROC曲线分析显示,SUA对ACS患者治疗后6个月内再入院事件的曲线下面积为0.649,95%*CI* 0.568~0.730,表明SUA对ACS患者治疗后6个月内再入院有一定的预测价值(图1)。

3 讨 论

本研究发现血清SUA水平升高增加ACS患者治疗后6个月内再入院风险,SUA对于ACS患者治疗后6个月内再入院风险有一定的预测价值。该发现或许能帮助临床医师在治疗策略和医院资源配置方面做出合理决策,且可改善ACS患者的预后、减少心血管不良事件。

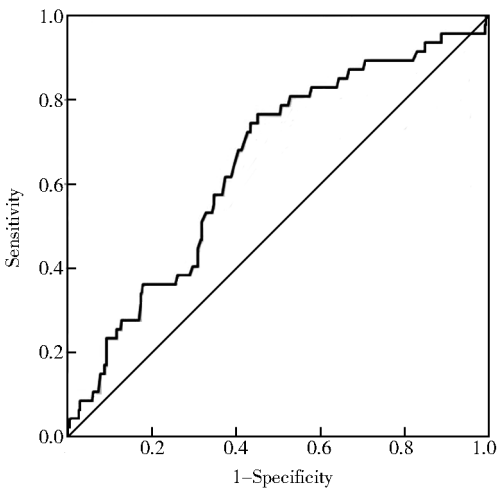

图 1 血清尿酸预测 ACS 患者 6 个月内再入院事件的 ROC 曲线

Figure 1 ROC curve of serum uric acid predicting readmission events within 6 months in ACS patients

ACS: acute coronary syndrome; ROC: receiver operating characteristic.

本研究结果显示 ACS 患者治疗后 6 个月内再入院率为 10.17%(47/462)。有研究虽探讨了行 PCI 的 ACS 患者 6 个月内再住院的影响因素,但没有表明具体的再入院率[8]。同时发现治疗方式、SUA、住院期间是否有不良事件和他汀类药物是否使用均在再入院组和非再入院组间具有显著性差异,提示诸多危险因素可导致再入院,对 ACS 患者的院外管理应是多因素综合干预。

近年来 SUA 作为冠心病的危险因素逐渐受到关注,既往研究提示随着 SUA 水平的增加,冠心病患病风险显著升高[9]。本研究进一步证实 SUA 水平的升高与 ACS 患者治疗后 6 个月内再入院相关,提示在规范二级预防的 ACS 患者中,仍需控制 SUA 水平。SUA 水平的升高对 ACS 患者治疗 6 个月内再入院风险的机制主要在于影响了血管内皮功能,已有研究表明 ACS 患者 SUA 水平升高与血管内皮功能障碍密切相关,血管内皮调节血管内稳态、血管舒缩张力、血管通透性、炎症和平滑肌细胞增殖,并整合多种功能,例如血压和凝血[11]。内皮功能障碍会导致血管壁内的动脉粥样硬化,可能导致 ACS 患者预后不良。本研究结果与新西兰的研究结果一致[6],随着 SUA 升高,包括再入院率在内的不良后果增加。SUA 与痛风之间密切相关[12,13],本研究发现 ACS 患者中的痛风人群的再入院率最高。在高 SUA 但未被确诊痛风的人群中,再入院率也高于正常 SUA 人群,说明 SUA 升高与 ACS 患者治疗后 6 个月内再入院相关。本研究首次探讨了 SUA 水平与 ACS 治疗后 6 个月再入院风险相关,该研究结果利于临床推广应用,可帮助医师识别再入院风险高的患者,改善预后。

本研究有一定局限性。首先,本研究为回顾性队列研究,且需收集患者体力活动、心理因素、社会经济因素等,这些因素可能影响 SUA 水平与再入院率。其次,患者再次住院就诊于不同医院,可能出现结果质控不一致的情况。

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(编辑:温玲玲)