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入院时血清钙水平与高血压性脑出血血肿体积、神经功能及预后的关系研究 *

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摘要 目的:探讨入院时血清钙水平与高血压性脑出血血肿体积、神经功能及预后的关系。**方法:**选择2018年9月-2020年4月我院收治的高血压性脑出血患者102例,根据患者入院时血清钙水平将其分为低血钙组(血清钙 <2.1 mmol/L, $n=34$)、正常血钙组(2.1 mmol/L $\leq$ 血清钙 ≤ 2.7 mmol/L, $n=39$)和高血钙组(血清钙 >2.7 mmol/L, $n=29$),比较各组性别、血肿体积、入院美国国立卫生研究院卒中量表(NIHSS)评分等临床资料。所有患者随访1年,观察患者格拉斯哥预后量表(GOS)评分,根据患者预后情况将患者分为预后良好组($n=84$)和预后不良组($n=18$),比较两组血清钙、血肿体积、入院NIHSS评分、GOS评分。应用受试者工作特征(ROC)曲线分析血清钙水平对患者预后的预测价值。**结果:**三组血肿体积、入院NIHSS评分、GOS评分、1年病死率、1年再出血率、总预后不良率比较有统计学差异($P<0.05$)。预后不良组血清钙水平、GOS评分显著低于预后良好组,血肿体积、入院NIHSS评分显著高于预后良好组($P<0.05$)。Pearson相关性分析显示:高血压性脑出血患者入院时血清钙水平与脑出血血肿体积、入院NIHSS评分呈负相关,与GOS评分呈正相关($P<0.05$)。ROC曲线分析显示入院时血清钙预测高血压脑出血不良预后的曲线下面积为0.129(95%CI:0.073~0.179)。**结论:**高血压性脑出血患者入院时血清钙水平与血肿体积、神经功能及预后存在一定关联,且入院时血清钙对高血压性脑出血不良预后具有一定预测价值。

关键词:高血压性脑出血;血清钙;血肿;神经功能;预后

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Relationship Study between Serum Calcium Level at Admission and Hematoma Volume, Neurological Function and Prognosis of Hypertensive Intracerebral Hemorrhage*

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ABSTRACT Objective: To investigate the relationship between the serum calcium level at admission and hematoma volume, neurological function and prognosis of hypertensive intracerebral hemorrhage. **Methods:** 102 patients with hypertensive intracerebral hemorrhage who were admitted to our hospital from September 2018 to April 2020 were selected, which were divided into low blood calcium group (serum calcium <2.1 mmol/L, $n=34$), normal blood calcium group (2.1 mmol/L $\leq$ serum calcium ≤ 2.7 mmol/L, $n=39$) and high blood calcium group (serum calcium >2.7 mmol/L, $n=29$) according to their serum calcium level at admission. The gender, hematoma volume, National Institutes of Health Stroke Scale (NIHSS) score at admission and other clinical data of each group were compared. All patients were followed up for 1 year, the Glasgow Outcome Scale (GOS) score of patients were observed. According to the prognosis of patients, the patients were divided into good prognosis group ($n=84$) and poor prognosis group ($n=18$). Serum calcium, hematoma volume, NIHSS score at admission and GOS score were compared between the two groups. Receiver operating characteristic (ROC) curve was used to analyze the predictive value of serum calcium level in patients' prognosis. **Results:** There were significant differences in hematoma volume, NIHSS score at admission, GOS score, 1-year fatality rate, 1-year rebleeding rate and overall poor prognosis rate in the three groups ($P<0.05$). The serum calcium level and GOS score in the poor prognosis group were significantly lower than those in the good prognosis group, and the hematoma volume and NIHSS score at admission were significantly higher than those in the good prognosis group ($P<0.05$). Pearson correlation analysis showed that the serum calcium level at admission of patients with hypertensive intracerebral hemorrhage was negatively correlated with hematoma volume, NIHSS score at admission, while positively correlated with GOS score ($P<0.05$). ROC curve analysis showed that the area under the curve for serum calcium at admission to predict adverse prognosis of hypertensive intrac-

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erebral hemorrhage was 0.129 (95%CI: 0.073-0.179). **Conclusion:** Serum calcium level at admission is correlated with hematoma volume, neurological function and prognosis in patients with hypertensive intracerebral hemorrhage, and serum calcium at admission has a certain predictive value for the poor prognosis of hypertensive intracerebral hemorrhage.

Key words: Hypertensive intracerebral hemorrhage; Serum calcium; Hematoma; Nerve function; Prognosis

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前言

高血压性脑出血是因高血压而引发的脑出血,约占脑出血的70%~80%,是神经内科的常见病与多发病^[1]。该病病情变化快,致残率和病死率均较高,临床预后较差。目前临床上对于高血压性脑出血主张早期治疗,以降低患者神经系统的损害。而早期对患者预后进行判断对于指导临床治疗具有重要意义。钙是人体重要的矿物质,在维持神经系统稳定性和血脑屏障稳定性中发挥重要作用^[2]。近年来研究发现,部分高血压性脑出血患者会出现血清钙水平的降低^[3,4]。且血清钙离子可以影响血管平滑肌功能、凝血功能及细胞稳态,可能与高血压性脑出血患者神经功能及预后情况密切相关^[5]。另外血肿体积是影响此类疾病进程和患者预后的重要因素^[6]。但目前对于血清钙水平与高血压性脑出血血肿体积、神经功能及预后的关系仍未完全明确。故本研究探讨入院时血清钙水平与高血压性脑出血血肿体积、神经功能及预后的关系,现报道如下。

1 资料与方法

1.1 一般资料

选择2018年9月-2020年4月我院收治的高血压性脑出血患者102例。纳入标准:(1)所有患者符合《中国脑出血诊治指南(2014)》中高血压性脑出血诊断标准^[7];(2)患者初次发生脑出血,年龄>18岁;(3)患者入院至发病时间≤24h,入院时接受血清钙水平检测;(4)患者病历资料完整,患者及家属对研究知情同意。排除标准:(1)合并心、肝、肾功能障碍或多器官功能衰竭者;(2)妊娠哺乳期妇女;(3)出血部位仅局限为蛛网膜下腔、脑室部位;(4)因脑血管畸形或颅内动脉瘤引发脑出血者;(5)未完成随访及不能配合实验研究者。男性59例,女性43例,年龄45~80岁,平均年龄(61.23±8.95)岁;高血压病史3~14年,平均(8.85±2.17)年;患者入院至发病时间3~24h,平均(6.37±0.89)h;收缩压140~180 mmHg,平均(164.05±12.77)mmHg,舒张压90~120 mmHg,平均(108.40±8.49)mmHg。根据患者入院时血清钙水平将其分为低血钙组(血清钙<2.1 mmol/L)34例,正常血钙组(2.1 mmol/L≤血清钙≤2.7 mmol/L)39例和高血钙组(血清钙>2.7 mmol/L)29例,本研究经医院伦理委员会批准。

1.2 方法

1.2.1 血肿体积的评估 所有患者入院后进行头颅CT检查,应用多田公式计算血肿体积:测量血肿最大截面最长直径A(cm),垂直与A线的宽度B(cm)及血肿出血层面厚度C(cm),血肿体积=A×B×C/2^[8]。

1.2.2 神经功能检测 所有患者入院后进行美国国立卫生研究院卒中量表(NIHSS)评分,该量表包括意识状态、语言、运动

功能、感觉、眼球运动、视野、共济运动等维度,满分42分,评分越高表明患者神经功能受损越严重^[9]。

1.2.3 血清钙水平检测 所有患者于入院24h内采集外周静脉血2 mL,经3500 r/min、离心半径12 cm离心5 min,分离血清取上清保存待测,应用美国贝克曼库尔特公司生产的AU5800全自动生化分析仪检测血清钙水平,正常参考值为2.1 mmol/L≤血清钙≤2.7 mmol/L^[10]。

1.2.4 随访与预后评估 所有患者随访1年,以患者死亡或随访日期截止(2021年5月31日)作为终止随访事件,统计患者1年病死率、1年再出血率,并计算总预后不良率。计算患者格拉斯哥预后量表(GOS)评分,该评分包括总分5分,其中:5分:痊愈或轻度残疾,患者可正常生活、工作;4分:中度残疾,但患者可独立生活,可以在保护下进行工作;3分:重度残疾,不能独立完成日常生活,需要照料;2分:植物生存;1分:死亡。3分及以下为预后不良,将预后不良者作为预后不良组,其余患者作为预后良好组^[11]。

1.3 统计学处理

应用SPSS28.0统计软件进行数据分析。计数资料以率(%)表示,实施卡方检验。计量资料经K-S检验符合正态分布且具备方差齐性,用($\bar{x} \pm s$)表示,两组间比较实施独立样本t检验,多组间比较采用LSD-t检验及单因素方差分析。相关性分析采用Pearson检验。应用受试者工作特征(ROC)曲线分析血清钙水平对高血压性脑出血患者预后的预测价值, $P<0.05$ 表明差异具有统计学意义。

2 结果

2.1 三组基线资料比较

三组性别、年龄、入院至发病时间、收缩压、舒张压比较无统计差异($P>0.05$),见表1。

2.2 三组血肿体积、入院NIHSS评分、GOS评分、1年病死率、1年再出血率、总预后不良率比较

三组血肿体积、入院NIHSS评分、GOS评分、1年病死率、1年再出血率、总预后不良率比较有统计学差异($P<0.05$),低血钙组血肿体积、入院NIHSS评分、1年病死率、再出血率、总预后不良率显著高于正常血钙组、高血钙组,GOS评分显著低于正常血钙组、高血钙组($P<0.05$),正常血钙组血肿体积、入院NIHSS评分显著高于高血钙组($P<0.05$),见表2。

2.3 不同预后患者血清钙、血肿体积、入院NIHSS评分、GOS评分比较

预后不良组血清钙水平、GOS评分显著低于预后良好组,血肿体积、入院NIHSS评分显著高于预后良好组($P<0.05$),见表3。

表 1 三组基线资料比较

Table 1 Comparison of baseline data of the three groups

Groups	n	Male/female	Age(years)	Time from admission to onset(h)	Systolic pressure (mmHg)	Diastolic pressure (mmHg)
Low blood calcium group	34	19/15	61.47± 6.98	6.97± 0.67	164.05± 9.98	107.88± 7.12
Normal blood calcium group	39	23/16	60.88± 7.54	6.11± 0.55	164.82± 10.11	108.31± 7.45
High blood calcium group	29	17/12	61.42± 6.72	6.02± 0.62	163.01± 9.79	109.12± 7.21
χ^2 or F		0.081	0.102	0.138	0.196	0.454
P		0.960	0.945	0.832	0.906	0.751

表 2 三组血肿体积、入院 NIHSS 评分、GOS 评分、1 年病死率、1 年再出血率、总预后不良率比较

Table 2 Comparison of hematoma volume, NIHSS score at admission, GOS score, 1-year fatality rate, 1-year rebleeding rate and overall poor prognosis rate in the three groups

Groups	n	Hematoma volume(ml)	NIHSS score at admission (scores)	GOS score (scores)	1-year fatality rate [n(%)]	1-year rebleeding rate [n(%)]	Overall poor prognosis rate [n(%)]
Low blood calcium group	34	15.01± 2.74* [#]	15.78± 4.28* [#]	3.02± 0.34* [#]	9(26.47)* [#]	6(17.65)* [#]	12(35.29)* [#]
Normal blood calcium group	39	11.06± 2.42 [#]	11.98± 4.14 [#]	4.21± 0.45	3(7.69)	1(2.56)	4(10.26)
High blood calcium group	29	9.44± 2.01	9.98± 4.11	4.28± 0.43	1(3.45)	1(3.45)	2(6.90)
F or χ^2		13.913	15.027	4.853	8.909	6.800	11.058
P		0.000	0.000	0.039	0.012	0.033	0.004

Note: * compared with normal blood calcium group $P<0.05$, # compared with high blood calcium group $P<0.05$.

表 3 不同预后患者血清钙、血肿体积、入院 NIHSS 评分、GOS 评分比较($\bar{x} \pm s$)

Table 3 Comparison of serum calcium, hematoma volume, NIHSS score and GOS score in patients with different prognosis($\bar{x} \pm s$)

Groups	n	Serum calcium (mmol/L)	Hematoma volume (mL)	NIHSS score at admission(scores)	GOS score (scores)
Poor prognosis group	18	1.78± 0.18	16.72± 2.01	17.29± 2.98	2.04± 0.18
Good prognosis group	84	2.45± 0.22	10.89± 3.03	11.69± 4.82	4.22± 0.51
t		-12.069	7.778	4.728	-17.920
P		0.000	0.000	0.000	0.000

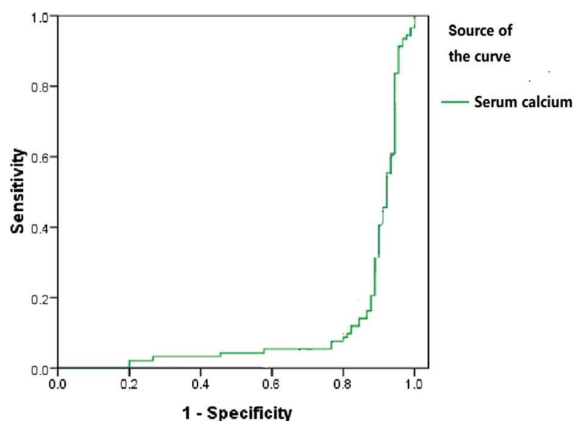


图 1 入院时血清钙水平对高血压性脑出血患者预后预测价值的 ROC 曲线

Fig.1 ROC curve of the prognostic value of serum calcium level at admission to patients with hypertensive intracerebral hemorrhage

2.4 高血压性脑出血患者入院时血清钙水平与脑出血血肿体积、入院 NIHSS 评分、GOS 评分的相关性

Pearson 相关性分析显示：高血压脑出血患者入院时血清钙水平与脑出血血肿体积、入院 NIHSS 评分呈负相关，与 GOS 评分呈正相关($r=-0.536$ 、 -0.489 、 0.571 ， $P=0.012$ 、 0.005 、 0.000)。

2.5 入院时血清钙水平对高血压性脑出血患者预后预测价值的 ROC 曲线分析

以高血压性脑出血患者为样本，应用 ROC 曲线分析入院时血清钙水平对高血压性脑出血患者预后的预测价值，结果显示入院时血清钙预测高血压性脑出血不良预后的最佳临界值为 2.17 mmol/L，其敏感度为 85.23%，特异度为 79.12%，曲线下面积为 0.129(95%CI:0.073~0.179)。见图 1。

3 讨论

近年来随着人们生活方式的改变和生活节奏的加快，高血

压性脑出血发病率逐年升高,严重影响人们的健康与生活^[12]。高血压性脑出血的病情变化快,发病机制复杂,患者临床预后存在一定差异^[13]。目前关于影响高血压性脑出血预后的确切因素仍未完全明确,患者的血糖、血压、血肿量、合并症等均可能对预后造成影响^[14,15]。钙是人体重要的矿物质,也是维持神经系统稳定、调节机体血压、血液凝固状态、细胞状态的重要物质^[16-18]。

本研究结果发现入院时不同血清钙水平的高血压性脑出血患者血肿体积、入院NIHSS评分、GOS评分、1年病死率、1年再出血率、1年总预后不良率均存在明显差异,入院时低血钙患者会影响患者血肿体积、神经功能和临床预后。笔者分析钙离子可能通过以下几方面影响了血肿体积、神经功能和临床预后:(1)影响患者血压调控。研究表明,钙摄入量少的人群罹患高血压风险较高,低血钙可能通过影响血管内皮功能影响血压调控,导致患者血压调控机制异常,血肿体积增加^[19,20]。(2)影响血脑屏障稳定性。研究表明,钙离子水平会影响血脑屏障稳定性,当细胞外钙离子浓度降低时,会导致血脑屏障中细胞黏附中断,当发生高血压性脑出血后会严重影响神经功能^[21,22]。(3)影响凝血功能。钙离子是参与凝血过程的重要物质,参与组织因子的激活及血小板黏附过程^[23]。有研究表明,血清钙离子降低大鼠的血液凝固时间明显延长,推测入院时低血钙可能会影响凝血功能,导致血肿体积增加^[24,25]。(4)血清钙水平降低增加神经细胞凋亡。研究发现当发生高血压性脑出血时,可以导致神经细胞钙通道开放,引发钙离子内流,细胞内钙离子超载,引起神经细胞凋亡^[26]。

本研究还对不同预后的高血压性脑出血患者进行了比较,结果发现预后不良组血清钙水平显著低于预后良好组,进一步证实了血清钙水平降低会导致高血压性脑出血患者预后不良。既往认为,高血压性脑出血在多种因素的作用下是一种短暂的出血过程,出血通常会在1 h内停止^[27]。但随着影像学技术的不断发展,人们发现高血压性脑出血早期血肿扩大不仅会加重患者的病情还会对患者的预后带来严重影响^[28]。本研究结果表明,预后不良组血肿体积高于预后良好组,符合以上报道,提示血肿体积会影响高血压性脑出血患者预后。NIHSS评分、GOS评分是临床上常用的量表,其中NIHSS评分可以评价神经功能受损情况,而GOS评分主要评价脑创伤患者大脑功能状态和预后情况^[29,30]。本研究结果显示预后不良组入院NIHSS评分、GOS评分显著高于预后良好组,且高血压性脑出血患者入院时血清钙水平与脑出血血肿体积、入院NIHSS评分呈负相关,与GOS评分呈正相关,表明高血压性脑出血患者入院时血清钙水平越低患者神经功能受损越严重,临床预后越差。

本研究还对入院时血清钙水平对高血压性脑出血患者预后的预测价值进行了分析,结果显示入院时血清钙预测高血压性脑出血不良预后的最佳临界值为2.17 mmol/L,其敏感度为85.23%,特异度为79.12%。提示临床上可以通过对高血压性脑出血患者入院时血清钙水平的检测分析为患者预后进行评价,为临床治疗提供依据。

综上所述,高血压性脑出血患者入院时血清钙水平与脑出血血肿体积、NIHSS评分呈负相关,与GOS评分呈正相关,入院时血清钙水平越低则临床预后越差,检测患者入院时血清钙水平对高血压性脑出血不良预后具有一定预测价值。

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