

# 急性脑出血后血肿腔引流液及外周血 CRP、TNF- $\alpha$ 和 MMP-9 水平与脑水肿体积及临床预后的关系

冯天保<sup>1</sup>, 许超<sup>1</sup>, 陈真<sup>2</sup>

1. 延安大学附属医院心脑血管医院放射科, 陕西 延安 716000;

2. 延安市人民医院放射科, 陕西 延安 716000

**【摘要】** 目的 分析急性脑出血(ACH)后血肿腔引流液及外周血 C 反应蛋白(CRP)、肿瘤坏死因子 $\alpha$  (TNF- $\alpha$ )、基质金属蛋白酶 9 (MMP-9) 水平与脑水肿体积及患者临床预后的关系。方法 选取 2015 年 3 月至 2020 年 4 月延安大学附属医院心脑血管医院收治的 98 例 ACH 患者为研究对象, 检测其术后第 1 天、第 3 天血肿腔引流液及外周血 CRP、TNF- $\alpha$ 、MMP-9 水平, 通过头颅 CT 测得患者脑水肿体积, 采用 Pearson 相关性分析法分析 CRP、TNF- $\alpha$ 、MMP-9 与脑水肿体积的相关性, 按 3 个月后患者的格拉斯哥结局量表(GOS)评分分为预后不良组( $n=56$ )与预后良好组( $n=42$ ), 使用 Logistic 回归分析法分析影响患者预后的危险因素。结果 术后第 3 天, 患者的脑水肿体积为(12.48 $\pm$ 2.05) mL, 大于术后第 1 天的(4.16 $\pm$ 0.57) mL, 差异有统计学意义( $P<0.05$ ); 术后第 3 天, 患者血肿腔引流液中的 CRP、TNF- $\alpha$  和 MMP-9 分别为(21.59 $\pm$ 3.63) mg/L、(167.56 $\pm$ 20.47) ng/L、(142.23 $\pm$ 23.38)  $\mu$ g/L, 明显高于术后第 1 天的(18.37 $\pm$ 2.35) mg/L、(119.18 $\pm$ 17.35) ng/L、(110.42 $\pm$ 19.86)  $\mu$ g/L, 差异均有统计学意义( $P<0.05$ ); 术后第 3 天, 患者外周血中的 CRP、TNF- $\alpha$  和 MMP-9 分别为(19.87 $\pm$ 2.85) mg/L、(159.04 $\pm$ 21.67) ng/L、(138.06 $\pm$ 22.45)  $\mu$ g/L, 明显高于术后第 1 天的(16.05 $\pm$ 2.24) mg/L、(112.36 $\pm$ 15.18) ng/L、(105.71 $\pm$ 16.24)  $\mu$ g/L, 差异均有统计学意义( $P<0.05$ ); 经 Pearson 相关性分析结果显示, 血肿腔引流液及外周血 CRP、TNF- $\alpha$ 、MMP-9 水平与脑水肿体积呈正相关( $P<0.05$ ); 预后不良组患者的脑出血量、脑水肿体积明显大于预后良好组, 血肿腔引流液及外周血的 CRP、TNF- $\alpha$ 、MMP-9 水平明显高于预后良好组, 差异均有统计学意义( $P<0.05$ ); 经 Logistic 回归分析结果显示, 血肿腔引流液及外周血 CRP、TNF- $\alpha$ 、MMP-9、出血量、脑水肿体积均为影响预后独立的危险因素( $P<0.05$ )。结论 ACH 后血肿腔引流液及外周血 CRP、TNF- $\alpha$ 、MMP-9 表达水平与脑水肿体积呈显著正相关, 且为患者预后危险因素。

**【关键词】** 急性脑出血; 脑水肿; C 反应蛋白; 肿瘤坏死因子 $\alpha$ ; 基质金属蛋白酶 9; 相关性

**【中图分类号】** R743.34 **【文献标识码】** A **【文章编号】** 1003-6350(2023)09-1233-05

**Relationship of CRP, TNF- $\alpha$ , and MMP-9 in hematoma cavity drainage fluid and peripheral blood after acute cerebral hemorrhage with cerebral edema volume and clinical prognosis.** FENG Tian-bao<sup>1</sup>, XU Chao<sup>1</sup>, CHEN Zhen<sup>2</sup>.

1. Department of Radiology, Cardiovascular Hospital, Affiliated Hospital of Yan'an University, Yan'an 716000, Shaanxi, CHINA; 2. Department of Radiology, Yan'an People's Hospital, Yan'an 716000, Shaanxi, CHINA

**【Abstract】 Objective** To analyze the relationship of C-reactive protein (CRP), tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), and matrix metalloproteinase 9 (MMP-9) levels in hematoma cavity drainage fluid and peripheral blood after acute cerebral hemorrhage (ACH) with cerebral edema volume and clinical prognosis. **Methods** A total of 98 patients with ACH who were admitted to Cardiovascular Hospital, Affiliated Hospital of Yan'an University from March 2015 to April 2020 were selected as the study subjects. The levels of CRP, TNF- $\alpha$ , and MMP-9 in hematoma cavity drainage fluid and peripheral blood were detected on the 1<sup>st</sup>, 3<sup>rd</sup> day after operation. The cerebral edema volume was measured by head CT. The correlation of CRP, TNF- $\alpha$ , and MMP-9 with cerebral edema volume was analyzed by Pearson correlation analysis. Three months later, the patients were divided into poor prognosis group ( $n=56$ ) and good prognosis group ( $n=42$ ) according to the Glasgow Outcome Scale (GOS) score. Logistic regression analysis was performed to screen the risk factors for the prognosis. **Results** The cerebral edema volume on the 3<sup>rd</sup> day after operation was (12.48 $\pm$ 2.05) mL, significantly larger than (4.16 $\pm$ 0.57) mL on the 1<sup>st</sup> day after operation ( $P<0.05$ ). The levels of CRP, TNF- $\alpha$ , and MMP-9 in hematoma cavity drainage fluid on the 3<sup>rd</sup> day after operation were (21.59 $\pm$ 3.63) mg/L, (167.56 $\pm$ 20.47) ng/L, and (142.23 $\pm$ 23.38)  $\mu$ g/L, significantly higher than (18.37 $\pm$ 2.35) mg/L, (119.18 $\pm$ 17.35) ng/L, and (110.42 $\pm$ 19.86)  $\mu$ g/L on the 1<sup>st</sup> day after operation ( $P<0.05$ ). The levels of CRP, TNF- $\alpha$ , and MMP-9 in peripheral blood on the 3<sup>rd</sup> day after operation were (19.87 $\pm$ 2.85) mg/L, (159.04 $\pm$ 21.67) ng/L, and (138.06 $\pm$ 22.45)  $\mu$ g/L, significantly higher than (16.05 $\pm$ 2.24) mg/L,

基金项目: 陕西省延安大学附属医院资助项目(编号: Z2018LSXB009)。

第一作者: 冯天保(1989—), 男, 主治医师, 主要研究方向为中枢神经系统疾病诊断与鉴别诊断。

通讯作者: 陈真(1988—), 男, 主治医师, 主要研究方向为骨疾病影像诊断, E-mail: chenzhen0904you@163.com。

(112.36±15.18) ng/L, and (105.71±16.24) μg/L on the 1<sup>st</sup> day after operation ( $P<0.05$ ). Pearson correlation analysis found that the levels of CRP, TNF-α, and MMP-9 in hematoma cavity drainage fluid and peripheral blood were positively correlated with cerebral edema volume ( $P<0.05$ ). The bleeding volume and cerebral edema volume of the poor prognosis group were larger than those of the good prognosis group. The levels of CRP, TNF-α, and MMP-9 in hematoma cavity drainage fluid and peripheral blood were significantly higher than those in the good prognosis group ( $P<0.05$ ). Logistic regression analysis found that CRP, TNF-α, and MMP-9 in hematoma cavity drainage fluid and peripheral blood, blood loss, and cerebral edema volume were independent prognostic risk factors ( $P<0.05$ ). **Conclusion** After ACH, the expression levels of CRP, TNF-α, and MMP-9 in hematoma cavity drainage fluid and peripheral blood are significantly positively correlated with cerebral edema volume, and they are prognostic risk factors.

**【Key words】** Acute cerebral hemorrhage; Cerebral edema; C-reactive protein; Tumor necrosis factor alpha; Matrix metalloproteinase 9; Correlation

急性脑出血(acute cerebral hemorrhage, ACH)为临床常见疾病,具有发病率及病死率高的特点,可对人类健康造成严重威胁<sup>[1]</sup>。有调查显示,ACH患者病死率可高达50%<sup>[2]</sup>。ACH引起的周围组织水肿与相应神经元损伤属于患者病情和临床预后主要影响因素<sup>[3]</sup>。有研究认为,脑出血后出现的脑组织水肿通常为微血管通透性升高及炎症反应所致<sup>[4]</sup>。脑出血患者脑组织损伤后可促使内皮细胞、胶质细胞以及星形细胞等合成肿瘤坏死因子α(tumor necrosis factor α, TNF-α)及其他炎性因子,该类因子可对人体炎性效应分子起到诱导作用,从而参与患者病理及生理反应<sup>[5]</sup>。相关报道称,基质金属蛋白酶9(matrix metalloprotein 9, MMP-9)水平和脑微血管通透性密切相关,可能参与脑水肿形成过程及病情进展<sup>[6]</sup>。既往文献指出,ACH患者C反应蛋白(C-reactive protein, CRP)表达水平与脑出血存在显著相关性,且属于预后影响因素<sup>[7]</sup>。目前,关于血肿腔引流液中炎症因子与ACH患者预后关系的报道鲜少。本文主要探究ACH后血肿腔引流液及外周血CRP、TNF-α、MMP-9水平与脑水肿体积及患者临床预后的关系,以期ACH病情与预后评估提供一定指导依据。

## 1 资料与方法

1.1 一般资料 选取2015年3月至2020年4月延安大学附属医院心脑血管医院收治的98例ACH患者进行前瞻性研究。纳入标准:(1)与ACH诊断标准<sup>[8]</sup>相符,且通过影像学检查(比如CT/磁共振成像)证实;(2)年龄18~70岁;(3)脑内血肿>25 mL,首次发病,病程短于24 h,并在发病24 h内予以手术治疗;(4)具有手术适应证,同意手术。排除标准:(1)合并严重脏器(心肝肾肺等)病变或者炎症性疾病;(2)外伤、脑动脉瘤破裂以及血管畸形造成的脑出血;(3)合并凝血功能障碍、自身免疫性疾病及处于生理期患者;(4)近期接受过抗炎药物、免疫抑制剂等治疗;(5)颅内肿瘤患者;(6)对CT灌注造影剂过敏者。本研究经医院伦理委员会批准,所有患者均签署知情同意书。

1.2 研究方法 采用自制调查表收集所有患者入院时性别、年龄、体质量指数(body mass index, BMI)、病程、高血压、糖尿病、出血量、出血部位等临床资料。评估入院3个月后患者格拉斯哥结局量表(GOS)评分<sup>[9]</sup>,按照预后情况分为预后不良组(分值为1~3分)与预后良好组(分值为4~5分)。

1.3 检测方法 分别于术后第1天、第3天采集血肿腔引流液与晨起空腹状态外周血样本,并进行脑水肿体积测定。(1)引流液与血清样本指标检测:在无菌肝素钠管之中注入血肿腔引流液,将其静置30 min后进行离心处理(3 000 r/min,连续15 min),分离上清液,存储于-70℃冰箱之中待测;外周血样本离心处理后(2 500 r/min,连续10 min)分离血清,置于-27℃环境中存储待测。通过酶联免疫吸附法进行引流液与血清样本内CRP、TNF-α、MMP-9水平测定,采用Abcam中国公司提供的试剂盒,检测过程严格依据试剂盒操作说明书完成。(2)脑水肿体积测定:通过Image-Pro Plus软件计算头颅CT图像呈现的脑水肿体积,选择明显水肿区域,予以CT灌注成像,同时和对侧脑白质具体灌注参数进行配对 $t$ 检验,从而提高诊断准确性。利用图像分析软件测定不同层面脑水肿面积大小,然后乘以层高,获得脑水肿体积。

1.4 统计学方法 利用SPSS22.0统计软件进行数据分析。计数资料比较采用 $\chi^2$ 检验;计量资料符合正态分布,以均数±标准差( $\bar{x}\pm s$ )表示,组间比较采用独立样本 $t$ 检验,术后不同时间的计量数据比较采用配对样本 $t$ 检验;采用Pearson相关性分析法分析CRP、TNF-α、MMP-9与脑水肿体积的相关性;采用Logistic回归分析法分析预后危险因素。以 $P<0.05$ 为差异有统计学意义。

## 2 结果

2.1 不同时间点血肿腔引流液CRP、TNF-α、MMP-9比较 术后第3天,患者血肿腔引流液中的CRP、TNF-α、MMP-9水平明显高于第1天,差异均有统计学意义( $P<0.05$ ),见表1。

表 1 不同时间点血肿腔引流液 CRP、TNF- $\alpha$ 、MMP-9 比较( $\bar{x}\pm s$ )

**Table 1 Comparison of CRP, TNF- $\alpha$ , and MMP-9 in hematoma cavity drainage fluid at different time points ( $\bar{x}\pm s$ )**

时间	例数	CRP (mg/L)	TNF- $\alpha$ (ng/L)	MMP-9 ( $\mu$ g/L)
术后第 1 天	98	18.37 $\pm$ 2.35	119.18 $\pm$ 17.35	110.42 $\pm$ 19.86
术后第 3 天	98	21.59 $\pm$ 3.63	167.56 $\pm$ 20.47	142.23 $\pm$ 23.38
<i>t</i> 值		-10.661	-25.327	-14.565
<i>P</i> 值		0.001	0.001	0.001

2.2 不同时间点外周血 CRP、TNF- $\alpha$ 、MMP-9 及脑水肿体积比较 术后第 3 天,外周血中 CRP、TNF- $\alpha$ 、MMP-9 水平及脑水肿体积较第 1 天明显增

大,差异均有统计学意义( $P<0.05$ ),见表 2。

2.3 CRP、TNF- $\alpha$ 、MMP-9 与脑水肿体积的相关性 经 Pearson 相关性分析结果显示,血肿腔引流液及外周血 CRP、TNF- $\alpha$ 、MMP-9 与脑水肿体积呈正相关( $P<0.05$ ),见表 3。

2.4 不同预后患者的临床资料比较 预后不良组患者的出血量、脑水肿体积明显大于预后良好组,血肿腔引流液及外周血的 CRP、TNF- $\alpha$ 、MMP-9 水平明显高于预后良好组,差异均有统计学意义( $P<0.05$ ),见表 4。

表 2 不同时间点外周血 CRP、TNF- $\alpha$ 、MMP-9 及脑水肿体积比较( $\bar{x}\pm s$ )

**Table 2 Comparison of peripheral blood CRP, TNF- $\alpha$ , MMP-9, and brain edema volume at different time points ( $\bar{x}\pm s$ )**

时间	例数	CRP (mg/L)	TNF- $\alpha$ (ng/L)	MMP-9 ( $\mu$ g/L)	脑水肿体积(mL)
术后第 1 天	98	16.05 $\pm$ 2.24	112.36 $\pm$ 15.18	105.71 $\pm$ 16.24	4.16 $\pm$ 0.57
术后第 3 天	98	19.87 $\pm$ 2.85	159.04 $\pm$ 21.67	138.06 $\pm$ 22.45	12.48 $\pm$ 2.05
<i>t</i> 值		-14.859	-25.081	-16.555	-62.873
<i>P</i> 值		0.001	0.001	0.001	0.001

表 3 CRP、TNF- $\alpha$ 、MMP-9 与脑水肿体积的相关性

**Table 3 Correlation of CRP, TNF- $\alpha$ , MMP-9 with brain edema volume**

项目	分类	脑水肿体积	
		<i>r</i> 值	<i>P</i> 值
血肿腔引流液指标	CRP	0.623	0.001
	TNF- $\alpha$	0.597	0.001
	MMP-9	0.518	0.001
外周血指标	CRP	0.682	0.001
	TNF- $\alpha$	0.745	0.001
	MMP-9	0.604	0.001

表 4 不同预后患者的临床资料比较[例(%), $\bar{x}\pm s$ ]

**Table 4 Comparison of clinical data between patients with different prognosis [*n* (%),  $\bar{x}\pm s$ ]**

临床资料	预后不良组( <i>n</i> =56)	预后良好组( <i>n</i> =42)	$\chi^2/t$ 值	<i>P</i> 值
性别			0.014	0.905
男	34 (60.71)	25 (59.52)		
女	22 (39.29)	17 (40.48)		
年龄(岁)	41.32 $\pm$ 7.08	39.25 $\pm$ 6.94	1.444	0.152
BMI (kg/m <sup>2</sup> )	23.16 $\pm$ 2.34	23.25 $\pm$ 2.37	0.187	0.852
病程(h)	13.05 $\pm$ 2.17	12.96 $\pm$ 2.10	0.206	0.837
高血压	17 (30.36)	9 (21.43)	0.982	0.322
糖尿病	4 (7.14)	3 (7.14)	0.157	0.692
出血量(mL)	30.58 $\pm$ 3.15	28.23 $\pm$ 3.01	3.725	0.001
出血部位			0.854	0.836
小脑	21 (37.50)	18 (42.86)		
大脑半球	17 (30.36)	14 (33.33)		
脑干	12 (21.43)	7 (16.67)		
其他	6 (10.71)	3 (7.14)		
脑水肿体积(mL)	4.68 $\pm$ 1.05	3.48 $\pm$ 0.58	6.676	0.001
血肿腔引流液指标				
CRP (mg/L)	20.58 $\pm$ 3.76	15.42 $\pm$ 2.76	7.502	0.001
TNF- $\alpha$ (ng/L)	125.49 $\pm$ 20.53	110.77 $\pm$ 19.42	3.594	0.001
MMP-9 ( $\mu$ g/L)	118.35 $\pm$ 18.65	99.85 $\pm$ 16.17	5.140	0.001
外周血指标				
CRP (mg/L)	19.53 $\pm$ 3.24	11.41 $\pm$ 1.73	14.731	0.001
TNF- $\alpha$ (ng/L)	121.37 $\pm$ 20.58	100.35 $\pm$ 16.43	5.443	0.001
MMP-9 ( $\mu$ g/L)	113.64 $\pm$ 19.15	95.14 $\pm$ 16.62	5.004	0.001

2.5 影响患者预后的危险因素 经 Logistic 回归分析结果显示,血肿腔引流液及外周血 CRP、TNF- $\alpha$ 、MMP-9、出血量、脑水肿体积均是影响患者预后的独立危险因素( $P<0.05$ ),见表 5。

表 5 影响患者预后危险因素的 Logistic 回归分析

**Table 5 Logistic regression analysis of the risk factors for prognosis**

变量	回归系数	标准误	Wald $\chi^2$ 值	<i>P</i> 值	OR 值	95%CI
出血量	0.401	0.123	10.629	0.001	1.493	1.173~1.900
脑水肿体积	0.306	0.118	6.725	0.010	1.358	1.078~1.711
血肿腔引流液指标						
CRP	0.417	0.143	8.504	0.004	1.517	1.147~2.008
TNF- $\alpha$	0.382	0.130	8.635	0.003	1.465	1.136~1.890
MMP-9	0.312	0.146	4.567	0.033	1.366	1.026~1.819
外周血指标						
CRP	0.503	0.118	18.171	0.001	1.654	1.312~2.084
TNF- $\alpha$	0.498	0.113	19.422	0.001	1.645	1.319~2.053
MMP-9	0.601	0.247	5.920	0.015	1.824	1.124~2.960

### 3 讨论

CRP 不仅属于炎症反应产物,同时亦可加重机体损伤<sup>[10]</sup>。Frontera 等<sup>[11]</sup>研究表明,CRP 可使补体系统被激活,提高氧自由基释放水平,引起脑血管痉挛,导致脑血流减少。TNF- $\alpha$  生物学作用广泛,主要为巨噬细胞以及内皮细胞等合成,可以参与机体凝血、炎症以及免疫调节等过程<sup>[12]</sup>。有报道称,MMP-9 可促进炎性细胞因子侵入脑组织,从而加重出血损伤<sup>[13]</sup>。本研究中,相较于术后第 1 天,术后第 3 天血肿腔引流液及外周血 CRP、TNF- $\alpha$ 、MMP-9 水平明显升高。可能由于术后第 1 天患者血脑屏障破坏较轻,血肿里面 CRP、TNF- $\alpha$ 、MMP-9 入血量较少,而到术后第 3 天,机体激活状态的凝血酶原增多,导致血肿腔引流液及外周血 CRP、TNF- $\alpha$ 、MMP-9 水平迅速升高。

陈晟等<sup>[14]</sup>研究指出,血清 CRP 浓度测定可用于评估脑出血患者病情程度。本研究发现,血肿腔引流液及外周血 CRP 水平和脑水肿体积具有正相关性。分析原因,CRP 作为炎性相关蛋白,能够激活下游核因子  $\kappa$ B (nuclear factor kappa-B, NF- $\kappa$ B) 信号通路,加重脑组织炎性损伤,从而进一步加重脑组织水肿<sup>[15]</sup>。有研究表明,脑出血患者 MMP-9 水平异常升高,可能在脑水肿产生中发挥作用,能够用于评估脑出血患者血肿扩大<sup>[16]</sup>。本研究显示,血肿腔引流液及外周血 MMP-9 与脑水肿体积呈显著正相关,与上述观点一致。MMP-9 可能通过降解细胞外基质,使得细胞外基质内所含层黏蛋白、IV 型胶原以及纤维连接蛋白等减少,提高血管通透性,有效开放血脑屏障,从而导致血管源性脑水肿产生<sup>[17]</sup>。相关报道称,脑出血后相应神经组织 TNF- $\alpha$  水平升高,是局部炎症反应程度主要标志物<sup>[18]</sup>。Ding 等<sup>[19]</sup>研究表明, TNF- $\alpha$  不仅具有上调 MMP-9 酶原表达作用,同时也能促使其转化成为有活性的酶。本研究相关性分析显示,血肿腔引流液及外周血 TNF- $\alpha$  和患者脑水肿体积呈正相关。可能因为随着脑组织损伤程度加重,机体免疫反应越剧烈,使得巨噬细胞与淋巴细胞等大量激活,相关炎症因子(比如 TNF- $\alpha$ )分泌水平升高,炎症因子又能刺激中性粒细胞或者单核细胞形成大量氧自由基,引起广泛性脑损伤,导致血脑屏障通透性升高,加重脑水肿<sup>[20]</sup>。本研究 Logistic 回归分析发现,血肿腔引流液及外周血 CRP、TNF- $\alpha$ 、MMP-9 水平、出血量、脑水肿体积均为 ACH 预后危险因素。考虑到出血量越多、脑水肿体积越大、脑组织炎症反应越严重,患者病情越严重,故预后不良风险越大。早期检测血肿腔引流液及外周血 CRP、TNF- $\alpha$ 、MMP-9 水平,有利于指导 ACH 临床预后评估。

综上所述,ACH 后血肿腔引流液及外周血 CRP、TNF- $\alpha$ 、MMP-9 水平越高,脑水肿体积越大,患者临床预后不良风险越高,动态监测其表达水平变化可为预后评估提供重要指导。

#### 参考文献

- Gopal M, Gupta K, Preet Singh A, et al. 65-year-old with acute cerebral hemorrhage [J]. *Brain Pathol*, 2020, 30(2): 429-430.
- Lattanzi S, Brigo F, Trinka E, et al. Neutrophil-to-lymphocyte ratio in acute cerebral hemorrhage: a system review [J]. *Transl Stroke Res*, 2019, 10(2): 137-145.
- Chen L, Xu M, Yan S, et al. Insufficient cerebral venous drainage predicts early edema in acute intracerebral hemorrhage [J]. *Neurology*, 2019, 93(15): e1463-e1473.
- Toyoda K, Palesch YY, Koga M, et al. Regional differences in the response to acute blood pressure lowering after cerebral hemorrhage [J]. *Neurology*, 2021, 96(5): e740-e751.
- Yuan JX, Li CC, Xiu B. The relationship between serum tumor necrosis factor- $\alpha$ , nerve growth factor and the degree of cerebral edema and prognosis after acute cerebral hemorrhage [J]. *Chin J Mod Med*, 2020, 30(19): 35-39.
- 苑建鑫, 李萃萃, 修波. 血清肿瘤坏死因子- $\alpha$ , 神经生长因子与急性脑出血后脑水肿程度及预后的关系[J]. *中国现代医学杂志*, 2020, 30(19): 35-39.
- Liu XY, Zhen YF, Cui JZ, et al. Relationship between delayed cerebral edema after cerebral hemorrhage and serum MMP-9 levels in patients with hypertension and diabetes mellitus [J]. *Shandong Medical Journal*, 2017, 57(2): 63-65.
- 刘兴宇, 甄艳凤, 崔建忠, 等. 高血压合并糖尿病患者脑出血后迟发性脑水肿与血清 MMP-9 水平的关系[J]. *山东医药*, 2017, 57(2): 63-65.
- Zhou ZR, Zhao YH, Sun R, et al. Effects of Xingnaojing on serum high-sensitivity C-reactive protein and neuron-specific enolase in patients with acute cerebral hemorrhage: A protocol of systematic review and meta-analysis [J]. *Medicine (Baltimore)*, 2020, 99(45): e21379.
- Neurology Branch of Chinese Medical Association, Cerebrovascular Disease Group of Neurology Branch of Chinese Medical Association. Guidelines for diagnosis and treatment of cerebral hemorrhage in China (2019) [J]. *Chin J Neurol*, 2019, 52(12): 994-1005.
- 中华医学会神经病学分会, 中华医学会神经病学分会脑血管病学组. 中国脑出血诊治指南(2019)[J]. *中华神经科杂志*, 2019, 52(12): 994-1005.
- Shen J, Yang H. Correlation between small bone window microsurgery for hypertensive intracerebral hemorrhage and activities of daily living scale and Glasgow prognostic score at different operation timings [J]. *Chinese Journal of Gerontology*, 2017, 37(2): 354-356.
- 沈健, 杨华. 不同手术时机小骨窗显微手术治疗高血压脑出血与日常生活活动能力量表、格拉斯哥预后评分的相关性[J]. *中国老年学杂志*, 2017, 37(2): 354-356.
- Yang BH, He Q, Ding CY, et al. High-sensitivity C-reactive protein as a predictive factor of acute kidney injury following aneurysmal subarachnoid hemorrhage: a prospective observational study [J]. *Acta Neurochir (Wien)*, 2019, 161(9): 1783-1791.
- Frontera JA, Provencio JJ, Sehba FA, et al. The role of platelet activation and inflammation in early brain injury following subarachnoid hemorrhage [J]. *Neurocrit Care*, 2017, 26(1): 48-57.
- Lin C, Tang X, Shi ZY, et al. Serum tumor necrosis factor  $\alpha$  levels are associated with new ischemic brain lesions after carotid artery stenting [J]. *J Vasc Surg*, 2018, 68(3): 771-778.
- Dang B, Duan X, Wang Z, et al. A therapeutic target of cerebral hemorrhagic stroke: matrix metalloproteinase-9 [J]. *Curr Drug Targets*, 2017, 18(12): 1358-1366.
- Chen S, Qiu Z, Zheng SJ, et al. Effects of Xingnaojing injection combined with edaravone on serum CRP, BNP, D-dimer and coagulation function indexes in elderly patients with acute cerebral hemorrhage [J]. *Chinese Journal of Gerontology*, 2018, 38(14): 3353-3355.
- 陈晟, 邱政, 郑绍俭, 等. 醒脑静注射液联合依达拉奉对老年脑出血急性期患者血清 CRP、BNP、D-二聚体和凝血功能指标的影响[J]. *中国老年学杂志*, 2018, 38(14): 3353-3355.
- Zhang CY, Lu Z, Wang YH, et al. Mild hypothermia regulates the expression of AQP4 in the brain tissue of CPR rats and reduces cerebral edema through the p38MAPK signaling pathway [J]. *Chin Crit Care Med*, 2019, 31(4): 480-483.
- 张重阳, 吕喆, 王耀辉, 等. 亚低温通过 p38MAPK 信号通路调控 CPR 大鼠脑组织 AQP4 表达并减轻脑水肿[J]. *中华危重病急救医*

# 颈段椎管内肿瘤患者显微手术后的预后状况及其影响因素

魏文渊, 别小华, 薛俊刚

西安交通大学附属红会医院神经外科, 陕西 西安 710000

**【摘要】** **目的** 探讨颈段椎管内肿瘤患者显微手术后的预后状况及其影响因素。**方法** 回顾性分析 2016 年 4 月至 2022 年 3 月于西安交通大学附属红会医院神经外科行显微手术的 100 例颈段椎管内肿瘤患者的临床资料, 依据格拉斯哥预后评分(GOS)评估其预后状况, 依据预后状况将患者分为预后良好组(GOS 评分>3 分) 79 例和预后不良组(GOS 评分≤3 分) 21 例。比较两组患者的临床资料, 采用多因素 Logistic 回归法分析影响颈段椎管内肿瘤患者显微手术后预后的因素。**结果** 单因素分析结果显示, 年龄、手术方式、肿瘤直径与性质、肿瘤切除程度、术前肌力状况、术前 JOA 评分、神经电生理术中监测状况、术后应用激素均与颈段椎管内肿瘤患者显微术后的预后有关 ( $P<0.05$ ); 经多因素 Logistic 回归分析结果显示, 年龄超过 60 岁、肿瘤直径≥4 cm、恶性肿瘤、全椎板手术、肿瘤次切除、术前肌力<3 级、神经电生理术中未监测、术后不使用激素、术前 JOA 评分较低均为颈段椎管内肿瘤患者显微手术后预后不良的独立危险因素 ( $P<0.05$ )。**结论** 颈段椎管内肿瘤患者显微手术后预后状况良好, 预后不良的独立危险因素包括年龄>60 岁、术前肌力<3 级、恶性肿瘤、肿瘤直径≥4 cm、全椎板手术、肿瘤次切除、神经电生理术中无监测、术后不使用激素、术前 JOA 评分较低。

**【关键词】** 颈段椎管内肿瘤; 显微手术; 预后状况; 危险因素

**【中图分类号】** R738 **【文献标识码】** A **【文章编号】** 1003—6350(2023)09—1237—04

**Prognosis and influencing factors of patients with cervical intraspinal tumor after microsurgery.** WEI Wen-yuan, BIE Xiao-hua, XUE Jun-gang. Department of Neurosurgery, Honghui Hospital Affiliated to Xi'an Jiaotong University, Xi'an 710000, Shaanxi, CHINA

**【Abstract】 Objective** To investigate the prognosis and influencing factors of patients with cervical intraspinal tumors after microsurgery. **Methods** The clinical data of 100 patients with cervical intraspinal tumors who underwent microsurgery in Department of Neurosurgery, Honghui Hospital Affiliated to Xi'an Jiaotong University from April 2016 to March 2022 were retrospectively analyzed, and their prognosis was evaluated according to Glasgow prognostic score (GOS). According to the prognosis, the patients were divided into a good prognosis group (GOS score >3, 79 cases) and a poor prognosis group (GOS score ≤3 points, 21 cases). The clinical data of the two groups were compared, and the factors influencing the prognosis of patients with cervical intravertebral tumors after microsurgery were analyzed by multivariate Logistic regression. **Results** Univariate analysis showed that age, surgical method, tumor diameter and nature, degree of tumor resection, preoperative muscle strength, preoperative JOA score, intraoperative neurophysiological monitoring, and postoperative hormone use were all correlated with the prognosis of patients with cervical intravertebral tumor after microsurgery ( $P<0.05$ ). The results of multiple Logistic regression analysis showed that age over 60 years old,

基金项目: 国家自然科学基金(编号: 81702210)。

第一作者: 魏文渊(1987—), 男, 主治医师, 主要研究方向为面肌痉挛、三叉神经痛方面手术治疗。

通讯作者: 薛俊刚(1981—), 男, 硕士, 主治医师, 主要研究方向为颅内肿瘤及椎管内肿瘤手术治疗、颅脑损伤、脑出血及脑血管畸形与颅内动脉瘤等手术治疗, E-mail: xuejungang002@163.com。

\*\*\*\*\*

学, 2019, 31(4): 480-483.

[16] Xia M, Su Y, Fu J, et al. The use of serum matrix metalloproteinases in cerebral amyloid angiopathy-related intracerebral hemorrhage and cognitive impairment [J]. J Alzheimers Dis, 2021, 82(3): 1159-1170.

[17] Tang Z, Wang W, Liu Z, et al. Blocking ERK signaling pathway lowers MMP-9 expression to alleviate brain edema after traumatic brain injury in rats [J]. Journal of Southern Medical University, 2020, 40(7): 1018-1022.

[18] Zhang XW, Wu Y, Wang DK, et al. Expression changes of inflammatory cytokines TNF- $\alpha$ , IL-1 $\beta$  and HO-1 in hematoma surrounding brain areas after intracerebral hemorrhage [J]. J Biol Regul Homeost Agents, 2019, 33(5): 1359-1367.

[19] Ding XW, Sun X, Shen XF, et al. Propofol attenuates TNF- $\alpha$ -induced MMP-9 expression in human cerebral microvascular endothelial cells by inhibiting Ca<sup>2+</sup>/CAMK II/ERK/NF- $\kappa$ B signaling pathway [J]. Acta Pharmacol Sin, 2019, 40(10): 1303-1313.

[20] Zhang JX, Zhang YG, Zhao L, et al. Correlation between serum ICAM-1, MMP-9, TNF- $\alpha$ , IL-6 levels and edema brain tissue volume around hemorrhage in patients with acute cerebral hemorrhage [J]. Shandong Medical Journal, 2017, 57(27): 58-60.

张极星, 张艳国, 赵亮, 等. 急性期脑出血患者血清 ICAM-1、MMP-9、TNF- $\alpha$ 、IL-6 水平和出血灶周围水肿脑组织体积的相关性[J]. 山东医药, 2017, 57(27): 58-60.

(收稿日期: 2022-08-08)