doi: 10.3978/j.issn.2095-6959.2021.11.014
View this article at: https://dx.doi.org/10.3978/j.issn.2095-6959.2021.11.014

微创血肿清除术后IL–6、GFAP、S100A8/A9水平与自发性脑出血患者功能预后的关系及其预测价值

祁波[1]，冯凌云[1]，冒平[2]

(1. 杨凌示范区医院神经外科，西安 712100；2. 西安交通大学第一附属医院神经外科，西安 710061)

[摘　要]　**目的：**分析白细胞介素-6(interleukin-6，IL-6)、胶质纤维酸性蛋白(glial fibrillary acidic protein，GFAP)、钙结合蛋白S100A8/A9与微创血肿清除术后自发性脑出血(spontaneous intracerebral hemorrhage，sICH)患者功能预后的关系及其预测价值。**方法：**选取2016年1月至2018年12月杨凌示范区医院118例接受微创血肿清除术的基底节区sICH患者，根据发病1个月后的改良Rankin指数(modified Rankin scale，mRS)评分情况分为预后良好组(n=66)与预后不良组(n=52)。微创血肿清除术前及次日，检测患者血清中IL-6、GFAP、S100A8/A9水平。随后比较两组患者术前、术后IL-6、GFAP、S100A8/A9水平的差异，采用二元logistic回归分析上述指标与患者功能预后的关系，采用Spearman秩相关分析上述指标与mRS评分的相关性，采用受试者工作特征曲线(ROC曲线)分析上述指标对sICH患者功能预后的预测价值并采用Hanley & McNei检验对各指标的AUC进行比较。**结果：**预后不良组患者术前血清中IL-6、GFAP、S100A8/A9水平与预后良好组差异均无统计学意义(P>0.05)；术后血清中IL-6、GFAP、S100A8/A9水平均显著高于预后良好组，差异均有统计学意义(P<0.05)。二元logistic回归分析显示：术后IL-6、GFAP、S100A8/A9水平均为影响患者功能预后的独立因素(P<0.05)。Spearman秩相关分析显示：术后IL-6、GFAP、S100A8/A9水平均与mRS评分呈显著正相关(P<0.05)。ROC曲线分析结果显示，术后IL-6、GFAP、S100A8/A9水平及联合预测因子在预测微创血肿清除术后sICH患者功能预后中的AUC分别为0.817、0.770、0.819、0.928，差异均有统计学意义(P<0.05)，且采用联合预测因子进行预测的AUC及敏感度(80.8%)和特异度(92.4%)均最高。**结论：**微创血肿清除术后sICH患者的IL-6、GFAP、S100A8/A9水平可能影响其功能预后；联合应用术后IL-6、GFAP、S100A8/A9可用于该类患者功能预后的预测，值得临床推荐使用。

[关键词]　自发性脑出血；微创血肿清除术；功能预后；白细胞介素-6；胶质纤维酸性蛋白；S100A8/A9

Relationship between IL-6, GFAP, S100A8/A9 levels and functional prognosis of patients with spontaneous intracerebral hemorrhage and their predictive value after minimally invasive evacuation of hematoma

QI Bo[1], FENG Lingyun[1], MAO Ping[2]

(1. Department of Neurosurgery, Yangling Demonstration Area Hospital, Xi'an 712100; 2. Department of Neurosurgery, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, China)

收稿日期 (**Date of reception**)：2021–03–12
通信作者 (**Corresponding author**)：冯凌云，Email: 251305573@qq.com

Abstract **Objective:** To analyze the relationship between interleukin-6 (IL-6), glial fibrillary acidic protein (GFAP), calcium binding protein S100A8/A9 and functional prognosis of patients with sICH after the minimally invasive evacuation of hematoma and their predictive value. **Methods:** One hundred and eighteen patients with sICH in basal ganglia who underwent the minimally invasive evacuation of hematoma and hospitalized in our hospital from January 2016 to December 2018 were selected. According to the modified Rankin scale (mRS) 1 month after the onset, they were divided into a good prognosis group and a poor prognosis group, including 66 cases and 52 cases respectively. The levels of IL-6, GFAP and S100A8/A9 in serum were detected before and the next day after the minimally invasive evacuation of hematoma. And then the preoperative and postoperative levels of IL-6, GFAP and S100A8/A9 were compared between the two groups; the relationship between the above indicators and functional prognosis of patients was analyzed by Binary logistic regression analysis; the correlation between the above indexes and mRS score was analyzed by Spearman rank correlation analysis; the predictive value of the above indicators for the functional prognosis of sICH patients was analyzed by Receiver operating characteristic curve (ROC), and the AUC of each indicator was compared by Hanley & McNei test. **Results:** The preoperative serum levels of IL-6, GFAP and S100A8/A9 in patients of poor prognosis group had no significantly differences with those of good prognosis group (P>0.05). The postoperative serum levels of IL-6, GFAP and S100A8/A9 in patients of poor prognosis group were significantly higher than those of good prognosis group (P<0.05). Binary logistic regression analysis showed that the postoperative levels of IL-6, GFAP, S100A8/A9 were independent factors of influencing functional prognosis for patients (P<0.05). Spearman rank correlation analysis showed that the postoperative levels of IL-6, GFAP, S100A8/A9 were significantly and positively correlated with mRS score (P<0.05). ROC curve analysis showed that the AUC of postoperative levels of IL-6, GFAP, S100A8/A9 and their combined predictors in predicting the functional prognosis of sICH patients after minimally invasive evacuation of hematoma were 0.817, 0.770, 0.819 and 0.928, respectively (P<0.05), and the AUC, sensitivity (80.8%) and specificity (92.4%) of combined predictors for prediction were the highest. **Conclusion:** The levels of IL-6, GFAP and S100A8/A9 after minimally invasive evacuation of hematoma may affect the functional prognosis of sICH patients. The combination of postoperative IL-6, GFAP and S100A8/A9 can be used to predict the functional prognosis of sICH patients, which is worthy of clinical recommendation.

Keywords spontaneous intracerebral hemorrhage; minimally invasive evacuation of hematoma; functional prognosis; interleukin-6; glial fibrillary acidic protein; S100A8/A9

脑出血(intracerebral hemorrhage，ICH)占急性脑卒中的10%~30%，其中自发性脑出血(spontaneous intracerebral hemorrhage，sICH)病情变化迅速，且部分患者病情隐匿加重，因此早期难以判断其预后[1]。因此，对sICH预后进行预测是临床研究的热点，不仅有助于临床治疗方案的选择，也有助于康复方案的制订[2-3]。

炎症反应所致脑组织损伤及微血管损伤是ICH后病情加重的主要原因之一[4-5]。白细胞介素-6(interleukin-6，IL-6)与ICH后出血灶周围水肿带的严重程度相关，是预后不良的独立危险因素[4,6]。星形胶质细胞在ICH的损伤过程中具有重要作用，胶质纤维酸性蛋白(glial fibrillary acidic protein，GFAP)可反映星形胶质细胞的活化程度，并作为星形胶质细胞骨架蛋白，参与对损伤区范围的限制，抑制炎症反应，进而参与ICH的修复，但过度表达时可能加重脑组织损伤[7-9]。钙结合蛋白S100A8/A9由激活的中性粒细胞或单核细胞分泌，可通过Toll样受体4(toll-like receptor 4，TLR4)激活其下游炎症信号通路，可能参与ICH后的炎症反应，并可用于预测预后[10-11]。因此，IL-6、GFAP与S100A8/A9不仅可能对ICH的预后产生影响，也可用于ICH患者功能预后的预测。由于目前对接受微创血肿清除术的基底节区sICH患者预后进行预测的研究较少，因此，我们对上述术后指标进行观察，以探索其与患者预后的关系及预测价值。

1 对象与方法

1.1 对象

采用随机数字表法，随机选取2016年1月至2018年12月杨凌示范区医院的118例sICH患者作为研究对象。入组对象均经头颅影像学检查确诊，并符合2015版AHA/ASA《自发性脑出血处理指南》[12]的sICH诊断标准。在118例患者中，男68例，女50例，年龄40~75(中位数61)岁。

纳入标准：1)首次发病；2)发病时间<24 h；3)年龄>18岁；4)出血量≥30 mL且为基底节区出血；5)均行微创血肿清除术；6)临床资料及随访资料完整。

排除标准：1)继发性脑出血如脑血管畸形、外伤等；2)既往脑血管病、颅脑外伤、颅内感染、颅内肿瘤等病史，以及颅脑手术病史者；3)慢性感染性疾病，或近期急性感染性疾病可能影响炎症反应指标者；4)长期口服激素或免疫抑制剂；5)严重脏器功能不全者；6)凝血功能异常，或使用抗血小板或抗凝药物者；7)肿瘤患者；8)微创血肿清除术手术禁忌证者；9)术前脑疝、脑出血破入脑室或伴梗阻性脑积水者；10)术中死亡或行心肺复苏者。

1.2 方法

1.2.1 分组

所有受试者发病1个月后进行改良Rankin指数(modified Ranking scale，mRS)[13-14]评分，该评分方法根据患者预后情况分为7个等级，分别为0分、1分、2分、3分、4分、5分、6分，其中0分为完全没有症状，6分为死亡，评分越高表明患者预后越差。将mRS评分≤2的66例患者设为预后良好组，3~6分的52例患者设为预后不良组。预后良好组：男38例，女28例；年龄40~73(中位数60.5)岁；发病至入院时间为(6.9±2.5) h；出血量(65.8±15.5) mL。预后不良组：男30例，女22例；年龄47~75(中位数62)岁；发病至入院时间为(7.1±2.4) h；出血量(64.1±15.1) mL。两组上述基线资料及其他资料如吸烟、饮酒、体重指数、既往病史(高血压、糖尿病、冠心病)等差异均无统计学意义(P>0.05)。本研究获杨凌示范区医院医学伦理委员会批准，并经患者家属知情同意。

1.2.2 检测指标

所有受试者术前及术后次日清晨空腹采集静脉血3 mL，离心后采集血清，于−80 ℃冰箱保存待测。采用化学发光法及配套试剂(Siemens，德国)检测血清IL-6水平，酶联免疫吸附试验双抗体夹心法及配套试剂盒(Rapidbio公司，美国)检测血清GFAP水平，酶联免疫吸附试验及配套试剂盒(南京森贝伽生物科技有限公司)检测血清S100A8/A9水平。操作均严格按照说明书中提供的步骤进行。

1.3 统计学处理

应用SPSS 21.0统计学软件进行数据分析。偏态分布资料用M(Q1，Q3)表示，两样本比较采用Mann-Whitney U检验。正态分布的计量资料用($\bar{x}$±s)表示，行方差齐性分析，方差齐两样本均数比较采用独立样本t检验，方差不齐则采用t'检验。计数资料用率表示，组间比较采用χ^2检验。多因素分析采用逐步回归的方法进行二元logistic回归分析。采用Spearman秩相关分析分析术后IL-6、GFAP、S100A8/A9水平与mRS评分的相关性。采用受试者工作特征曲线(receiver operating characteristic curve，ROC曲线)分析术后IL-6、GFAP、S100A8/A9值对sICH功能预后的预测价值，曲线下面积(area under curve，AUC)的比较采用Hanley & McNei检验(采用Medcalc软件分析)。P<0.05为差异有统计学意义。

2 结果

2.1 两组患者术后 IL-6、GFAP、S100A8/A9 水平

预后不良组患者术前血清中IL-6、GFAP、S100A8/A9水平与预后良好组的差异均无统计学意义(P>0.05)；预后不良组患者术后血清中IL-6、GFAP、S100A8/A9水平均显著高于预后良好组，差异均有统计学意义(P<0.05，表1)。

2.2 sICH 患者功能预后的 logistic 多因素分析

将术后IL-6、GFAP、S100A8/A9纳入sICH患者功能预后logistic多因素回归模型中(赋值：预后良好=0，预后不良=1)，结果显示：术后IL-6、GFAP、S100A8/A9水平均为接受微创血肿清除术的基底节区sICH患者功能预后的独立危险因素(表2)。

2.3 术后 IL-6、GFAP、S100A8/A9 水平与 mRS 评分的相关性

由Spearman秩相关分析可见：术后IL-6、GFAP、S100A8/A9水平与mRS评分均呈显著正相关(P<0.05，图1)。

表1 两组sICH患者术前及术后IL-6、GFAP、S100A8/A9水平比较

Table 1 Comparison of IL-6, GFAP and S100A8/A9 levels in two groups of sICH patients before and after operation

组别	*n*	IL-6/($ng \cdot L^{-1}$)		GFAP/($ng \cdot L^{-1}$)		S100A8/A9/($\mu g \cdot L^{-1}$)	
		术前	术后	术前	术后	术前	术后
预后良好组	66	25.58 ± 8.74	45.38 ± 11.95	12.34 ± 2.55	8.17 ± 2.34	19.37 ± 2.43	16.15 ± 2.18
预后不良组	52	25.36 ± 8.59	64.50 ± 16.78	12.31 ± 2.48	10.80 ± 2.75	19.36 ± 2.39	19.09 ± 2.51
t		0.137	−6.754	0.082	−5.612	0.011	−6.795
P		0.891	<0.001	0.934	<0.001	0.991	<0.001

表2 sICH患者功能预后logistic多因素分析

Table 2 Logistic multivariate analysis of functional prognosis in patients with sICH

变量	B	S.E.	Wald	df	*P*	OR	95%CI
IL-6	0.101	0.024	18.115	1	<0.001	1.107	1.056~1.160
GFAP	0.299	0.117	6.497	1	0.11	1.349	1.072~1.698
S100A8/A9	0.539	0.130	17.182	1	<0.001	1.714	1.328~2.211
常量	−17.978	3.298	29.717	1	<0.001	0.000	

模型检验：χ^2=82.694，*P*<0.001；拟合优度检验：χ^2=4.909，*P*=0.767。

Model test: χ^2=82.694, *P*<0.001; Goodness of fit test: χ^2=4.909, *P*=0.767.

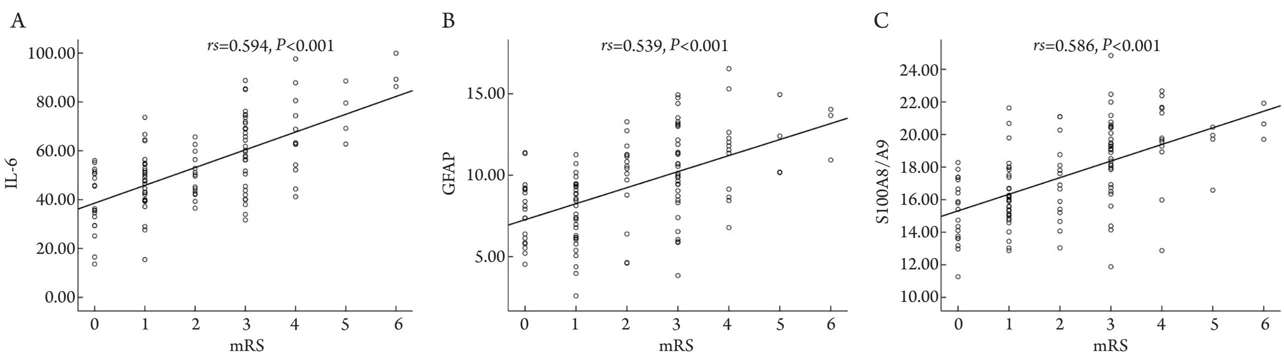

图1 术后IL-6、GFAP、S100A8/A9水平与mRS评分的相关性散点图

Figure 1 Scatter plot of correlation between the postoperative levels of IL-6, GFAP, S100A8/A9 and mRS score

(A)术后IL-6水平与mRS评分的相关性散点图；(B)术后GFAP水平与mRS评分的相关性散点图；(C)术后S100A8/A9水平与mRS评分的相关性散点图。

(A) Scatter plot of correlation between postoperative IL-6 level and mRS score; (B) Scatter plot of correlation between postoperative GFAP level and mRS score; (C) Scatter plot of correlation between postoperative S100A8/A9 level and mRS score.

2.4 术后IL-6、GFAP、S100A8/A9水平对sICH患者功能预后的预测效能分析

将术后IL-6、GFAP、S100A8/A9及联合预测因子共同纳入sICH患者功能预后预测的ROC曲线分析，可见术后IL-6、GFAP、S100A8/A9及联合预测因子在预测脑出血患者功能预后中的AUC分别为0.817、0.770、0.819、0.928，差异均有统计学意义(*P*<0.01)，其中联合预测因子的AUC显著高

于IL-6、GFAP、S100A8/A9(Z=3.307，P<0.001；Z=4.055，P<0.001；Z=2.879，P=0.004)。联合预测因子用于预测sICH患者功能预后的敏感度为80.8%，特异度为92.4%。提示术后IL-6、GFAP、S100A8/A9联合用于微创血肿清除术后基底节区sICH患者功能预后的预测价值最高(图2，表3、4)。

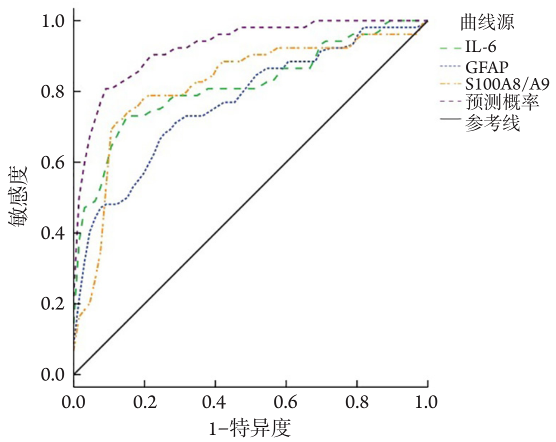

图2 术后IL-6、GFAP、S100A8/A9及联合预测因子用于功能预后预测的ROC曲线

Figure 2 ROC curves of postoperative IL-6, GFAP, S100A8/A9 and their combined predictors for predicting functional prognosis

表3 术后IL-6、GFAP、S100A8/A9及联合预测因子用于功能预后预测的ROC统计结果

Table 3 ROC statistical results of postoperative IL-6, GFAP, S100A8/A9 and their combined predictors in predicting functional prognosis

变量	AUC	标准误	P	渐近95%CI	最佳截断值
IL-6	0.817	0.041	<0.001	0.736~0.898	56.11
GFAP	0.770	0.044	<0.001	0.683~0.856	9.42
S100A8/A9	0.819	0.042	<0.001	0.738~0.901	18.32
联合预测因子	0.928	0.023	<0.001	0.883~0.973	0.57

表4 术后IL-6、GFAP、S100A8/A9单项及联合检测的诊断效能

Table 4 Diagnostic efficacy of single and combined detection of postoperative IL-6, GFAP and S100A8/A9

项目	敏感度/%	特异度/%
IL-6	73.1	86.4
GFAP	73.1	71.2
S100A8/A9	71.2	89.4
联合预测因子	80.8	92.4

3 讨论

sICH病情凶险，70%的患者可因早期血肿快速扩大导致病情急剧恶化，致使该病急性期病死率可高达30%~40%[15-16]。虽然针对基底节区超过30 mL的sICH患者，微创血肿清除术疗效较为肯定，但目前临床仍缺乏预测该类患者预后的有效方法。预判术后病情的进展情况，进而及时调整监测及治疗方法，可改善生存率及功能预后[17-18]。因此，研究术后功能预后的影响因素并探索其预测指标，具有重要的临床意义。

IL-6等炎症因子与脑出血的预后密切相关。研究发现[6,19-21]：IL-6与sICH患者的出血量及神经功能损伤相关，是周围水肿体积和出血后14 d神经功能的独立危险因素，且与高血压sICH患者的远期预后相关。但IL-6与微创血肿清除术后sICH患者预后的关系研究较少。GFAP在ICH后表达增加，近年来被证实可通过介导炎症反应，在ICH后的继发性损伤中发挥加重脑损害的作用，不仅与sICH血肿体积、周围水肿体积及预后呈正相关，且与

患者认知功能障碍有关，因此还可用于预测90 d神经功能预后，但其诊断敏感度并不理想[8,16,22-25]。钙结合蛋白S100A8/A9与心血管疾病关系较为密切，与冠状动脉粥样硬化斑块的形成有关，是心绞痛早期敏感的血清标志物之一；不仅参与了脑缺血再灌注损伤的进程，且其水平在接受微创血肿清除术且治疗有效的sICH患者中降低，因此可反映手术治疗的效果[26-28]。然而，GFAP及S100A8/A9与微创血肿清除术后sICH患者预后的关系及其预测价值尚不明确。

为研究IL-6、GFAP、S100A8/A9与微创血肿清除术后sICH患者功能预后的关系及其预测价值，本研究首先通过比较sICH不同预后情况术前、术后血清IL-6、GFAP、S100A8/A9水平，从单因素分析的角度探讨其对预后的影响。统计结果显示：预后不良组患者血清中术后IL-6、GFAP、S100A8/A9水平均显著高于预后良好组。随后通过Logistic回归分析发现术后IL-6、GFAP、S100A8/A9水平均为sICH患者功能预后的独立危险因素。

在IL-6在ICH中作用的研究中，李秋萌[29]通过向ICH模型小鼠转输Treg细胞，发现IL-6及肿瘤坏死因子-α(tumor necrosis factor-α，TNF-α)减少，而具有抗炎作用的IL-10增加，继而改善ICH后脑水肿程度，减少血肿量、降低了神经功能缺损评分。孟召友[30]研究发现：过表达A20基因可通过抑制E3泛素连接酶——肿瘤坏死因子受体相关蛋白6(TNF receptor associated factor 6，TRAF6)的表达，减少IL-1β、IL-6、TNF-α表达，并减少小鼠血肿周围组织神经元凋亡，促进血肿吸收并改善功能预后。过表达miR-132可能通过乙酰胆碱酯酶(acetylcholinesterase，AChE)发挥抗炎作用，进而减少IL-β、IL-6、TNF-α表达，并改善ICH小鼠预后[31]。在GFAP的相关研究中，钱红等[32]通过沉默表皮生长因子受体(epidermal growth factor receptor，EGFR)表达后发现：ICH模型大鼠血肿周围脑组织GFAP表达下降，脑水肿程度减轻，神经功能评分改善。杨慧等[33]通过过表达微小RNA let-7a后发现：ICH大鼠GFAP表达降低，神经元凋亡减少，病理损伤减轻，最终神经功能得以改善。针对S100A8/A9在ICH中的研究则较少，仅有少许研究[11]发现S100A8/A9水平是ICH患者30 d预后的危险因素。以上研究结果均提示，针对IL-6、GFAP、S100A8/A9水平进行干预，可能是改善ICH患者功能预后的潜在方法。然而，针对IL-6、GFAP、S100A8/A9水平进行干预，是否可能通过上述分子信号途径，改善微创血肿清除术后sICH患者的功能预后，仍有待进一步研究。

随后，本研究通过Spearman秩相关分析发现：sICH患者微创血肿清除术后的IL-6、GFAP、S100A8/A9水平均与mRS评分呈正相关；通过绘制ROC曲线发现：术后IL-6、GFAP、S100A8/A9水平及联合预测因子均可用于预测患者的功能预后，且联合预测的预测价值及敏感度、特异度均最优。以上结果提示：微创血肿清除术后，可联合应用术后IL-6、GFAP、S100A8/A9对sICH患者的预后进行预测，以帮助监测及治疗方案的制订、调整。

综上所述，微创血肿清除术后sICH患者的IL-6、GFAP、S100A8/A9水平可能影响其功能预后，对IL-6、GFAP、S100A8/A9进行干预有可能改善术后sICH患者的预后；联合应用术后IL-6、GFAP、S100A8/A9对患者的功能预后进行预测，可能有助于术后治疗方案的制订。然而，本研究的样本量相对不足，且未对IL-6、GFAP、S100A8/A9在手术前后的变化趋势进行观察，因此下一步将增加样本量并增加观察时点以深入研究。

参考文献

1. Patil A, Shree R, Naheed D, et al. Pearls & Oy-sters: paraneoplastic cerebral vasculitis: Rare cause of spontaneous convexity subarachnoid hemorrhage[J]. Neurology, 2018, 90(9): e815-e817.
2. Walter J, Unterberg AW, Zweckberger K. Lethal ultra-early subarachnoid hemorrhage due to rupture of de novo aneurysm 5 months after primary aneurysmatic subarachnoid hemorrhage[J]. World Neurosurg, 2018, 113: 316-319.
3. AlMatter M, Aguilar Péreza MA, Bhogal P, et al. Results of interdisciplinary management of 693 patients with aneurysmal subarachnoid hemorrhage: clinical outcome and relevant prognostic factors[J]. Clin Neurol Neurosurg, 2018, 167: 106-111.
4. 周洪霞, 娄宁, 魏子峰, 等. 大鼠脑出血后血肿周围脑水肿及其与NF-kB和IL-6表达的关系[J]. 山东大学学报(医学版), 2012, 50(11): 30-33.
ZHOU Hongxia, LOU Ning, WEI Zifeng, et al. Expressions of NF-kB and IL-6 around the hematoma and their correlations with cerebral edema after intracerebral hemorrhage in rats[J]. Journal of Shandong University. Health Science, 2012, 50(11): 30-33.
5. Zhu H, Wang Z, Yu J, et al. Role and mechanisms of cytokines in the secondary brain injury after intracerebral hemorrhage[J]. Prog Neurobiol, 2019, 178: 101610.

6. 廖鹏, 耿保伟, 张小翠, 等. 脑出血患者血清中IL-6和TNF-α水平与患者神经功能及脑水肿体积的关系[J]. 中华保健医学杂志, 2018, 20(5): 406-408.
LIAO Peng, GENG Baowei, ZHANG Xiaocui, et al. Relationship between serum IL-6 and TNF-αlevels and neurological function and volume of cerebral edema in patients with intracerebral hemorrhage[J]. Chinese Journal of Health Care and Medicine, 2018, 20(5): 406-408.
7. Ren C, Kobeissy F, Alawieh A, et al. Assessment of serum UCH-L1 and GFAP in acute stroke patients[J]. Sci Rep, 2016, 6: 24588.
8. Bhatia R, Warrier AR, Sreenivas V, et al. Role of blood biomarkers in differentiating ischemic stroke and intracerebral hemorrhage[J]. Neurol India, 2020, 68(4): 824-829.
9. Luger S, Jæger HS, Dixon J, et al. Diagnostic accuracy of glial fibrillary acidic protein and ubiquitin carboxy-terminal hydrolase-L1 serum concentrations for differentiating acute intracerebral hemorrhage from ischemic stroke[J]. Neurocrit Care, 2020, 33(1): 39-48.
10. 陈晓南, 王红艳, 赵洪宇, 等. 钙卫蛋白、TLR-4及MAPK信号转导途径在动脉血栓形成过程中与COX-2的关系[J]. 上海交通大学学报(医学版), 2016, 36(4): 474-480.
CHEN Xiaonan, WANG Hongyan, ZHAO Hongyu, et al. Correlation between calprotectin, TLR-4, and MAPK signal transduction pathways and COX-2 in the process of arterial thrombosis[J]. Journal of Shanghai Jiaotong University. Medical Science, 2016, 36(4): 474-480.
11. 夏芳芳. 血清S100A8/A9水平在新发脑出血患者功能预后中的预测价值[D]. 汕头: 汕头大学, 2014.
XIA Fangfang. The predictive value of S100A8/A9 level in the function outcome of first intracerebral hemorrhage[D]. Shantou: Shantou University, 2014.
12. Hemphill JC 3rd, Greenberg SM, Anderson CS, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association[J]. Stroke, 2015, 46(7): 2032-2060.
13. McArthur K, Fan YH, Pei Z, et al. Optimising outcome assessment to improve quality and efficiency of stroke trials[J]. Expert Rev Pharmacoecon Outcomes Res, 2014, 14(1): 101-111.
14. 范玉华, 姬晓昙, 蓝琳芳. 国内脑卒中临床试验疗效判断方法中改良Rankin评分的应用现状[J]. 中国神经精神疾病杂志, 2015, 41(7): 412-415.
FAN Yuhua, JI Xiaotan, LAN Linfang. The application of mRS in the methods of outcome assessment in Chinese stroke trials[J]. Chinese Journal of Nervous and Mental Diseases, 2015, 41(7): 412-415.
15. 李晓明, 郭永. 脑出血早期血肿扩大的影响因素及其与预后的关系[J]. 卒中与神经疾病, 2019, 26(5): 614-616, 629.
LI Xiaoming, GUO Yong. Influencing factors of hematoma enlargement in early stage of intracerebral hemorrhage and its relationship with prognosis[J]. Stroke and Nervous Diseases, 2019, 26(5): 614-616, 629.
16. 何磊磊, 孙正杰, 郭艳霞, 等. 血清胶质纤维酸性蛋白C反应蛋白及和肽素联合MICH评分在自发性脑出血患者预后判断中的价值[J]. 中国急救医学, 2016, 36(6): 502-506.
HE Leilei, SUN Zhengjie, GUO Yanxia, et al. The significance of serum glial fibrillary acidic protein, C -reactive protein and copeptin combined with MICH score in predicting prognosis of patients with spontaneous intracerebral hemorrhage[J]. Chinese Journal of Critical Care Medicine, 2016, 36(6): 502-506.
17. 王朝平, 吴杰, 周敏. 微创钻孔引流与开颅血肿清除术治疗中老年高血压脑出血的临床疗效及预后比较[J]. 中国老年学杂志, 2016, 36(18): 4494-4495.
WANG Zhaoping, WU Jie, ZHOU Min. Comparison of clinical efficacy and prognosis of minimally invasive drilling drainage and craniotomy hematoma clearance in the treatment of middle-aged and elderly patients with hypertensive intracerebral hemorrhage[J]. Chinese Journal of Gerontology, 2016, 36(18): 4494-4495.
18. 韩筅. 微创锥颅立体定向软通道置管血肿引流术与传统开颅血肿清除术治疗高血压基底核区出血临床效果的对比研究[J]. 实用心脑肺血管病杂志, 2019, 27(11): 69-72.
HAN Xiao. Clinical effect on hypertensive basal ganglia hemorrhage between minimally invasive stereospecific skull-drilling soft-channel hematoma drainage and traditional craniotomy for hematoma evacuation: a comparative study[J]. Practical Journal of Cardiac Cerebral Pneumal and Vascular Disease, 2019, 27(11): 69-72.
19. 陈琳, 周成芳, 梁江红. 高血压脑出血患者CRP IL-6水平及其临床意义[J]. 中国实用神经疾病杂志, 2016, 19(13): 39-41.
CHEN Lin, ZHOU Chengfang, LIANG Jianghong. CRP IL-6 level and its clinical significance in patients with hypertensive intracerebral hemorrhage[J]. Chinese Journal of Practical Nervous Diseases, 2016, 19(13): 39-41.
20. 申松波, 胡胜, 吴星, 等. 脑出血患者血清hs-CRP、IL-6水平与脑出血量及神经功能损伤的相关性[J]. 神经损伤与功能重建, 2020, 15(11): 652-653, 680.
SHEN Songbo, HU Sheng, WU Xing, et al. Correlation of serum hs-CRP, IL-6 levels with cerebral hemorrhage volume and neurological impairment in patients with cerebral hemorrhage[J]. Neural Injury and Functional Reconstruction, 2020, 15(11): 652-653, 680.
21. 张维, 李少泉, 彭文龙, 等. 血清IL-6、TNF-α、MMP-9、CRP水平与高血压脑出血患者预后的相关性分析[J]. 解放军医药杂志, 2020, 32(3): 105-108.
ZHANG Wei, LI Shaoquan, PENG Wenlong, et al. Correlation of serum IL-6, TNF-α, MMP-9 and CRP levels with prognosis in patients with hypertensive cerebral hemorrhage[J]. Medical & Pharmaceutical Journal of Chinese People's Liberation, 2020, 32(3): 105-108.
22. 王辉, 时代音, 胡春婷, 等. 丙戊酸钠联合尼莫地平治疗急性脑出血的疗效观察及对神经功能和TF、GFAP水平的影响[J]. 解放

军预防医学杂志, 2019, 37(8): 96-97.
WANG Hui, SHI Daiyin, HU Chunting, et al. Effect of sodium valproate combined with nimodipine in the treatment of acute cerebral hemorrhage and its influence on neurological function and TF, GFAP levels[J]. Journal of Preventive Medicine of Chinese People's Liberation Army, 2019, 37(8): 96-97.

23. 林涛, 周俊香, 杨菁, 等. 康复训练联合促红细胞生成素对脑出血大鼠神经修复及海马胶质原纤维酸性蛋白表达的影响[J]. 神经疾病与精神卫生, 2019, 19(6): 594-598.
LIN Tao, ZHOU Junxiang, YANG Jing, et al. Effects of rehabilitation training combined with erythropoietin on nerve repair and expression of GFAP in hippocampus of rats with cerebral hemorrhage[J]. Journal of Neuroscience and Mental Health, 2019, 19(6): 594-598.

24. 刘宇明, 邓燕华, 许治强, 等. 脑出血患者血清NSE、GFAP、BDNF水平变化与认知障碍相关性研究[J]. 脑与神经疾病杂志, 2016, 24(10): 623-626.
LIU Yuming, DENG Yanhua, XU Zhiqiang, et al. Correlation of serum levels of NSE, GFAP, BDNF and cognitive impairment in patients with intracerebral hemorrhage[J]. Journal of Brain and Nervous Diseases, 2016, 24(10): 623-626.

25. 熊维, 肖明跃, 张媚. 胶质细胞原纤维酸性蛋白诊断脑缺血性疾病的Meta分析[J]. 中国现代医学杂志, 2017, 27(14): 66-70.
XIONG Wei, XIAO Mingyue, ZHANG Mei. Value of serum GFAP in differential diagnosis of intracerebral hemorrhage and ischemic stroke: a systematic review and Meta-analysis[J]. China Journal of Modern Medicine, 2017, 27(14): 66-70.

26. 蒲志丹. S100A8/A9在急性动脉硬化性脑梗死患者血清中表达的研究[D]. 广州: 广州医科大学, 2017.
PU Zhidan. Study on the expression of S100A8/A9 in serum of patients with acute arteriosclerotic cerebral infarction[D]. Guangzhou: Guangzhou Medical University, 2017.

27. Wang C, Kou Y, Han Y, et al. Early serum calprotectin (S100A8/A9) predicts delayed cerebral ischemia and outcomes after aneurysmal subarachnoid hemorrhage[J]. J Stroke Cerebrovasc Dis, 2020, 29(5): 104770.

28. 赵东林, 熊超, 李德奎. 钻孔引流清除术对脑出血病人血清S100A8/A9水平及脑水肿的影响[J]. 中西医结合心脑血管病杂志, 2017, 15(13): 1656-1658.
ZHAO Donglin, XIONG Chao, LI Dekui. Effect of drilling drainage and clearance on serum S100A8/A9 level and brain edema in patients with cerebral hemorrhage[J]. Chinese Journal of Integrative Medicine on Cardio/Cerebrovascular Disease, 2017, 15(13): 1656-1658.

29. 李秋萌. Tregs通过IL-10/STAT3诱导小胶质细胞M2型极化减轻脑出血炎症损伤[D]. 重庆: 重庆医科大学, 2018.
LI Qiumeng. Regulatory T cells attenuate intracerebral hemorrhage-induced inflammatory injury by modulating microglia M2 polarization through the IL-10/STAT3 pathway[D]. Chongqing: Chongqing Medical University, 2018.

30. 孟召友. A20调控TRAF6聚泛素化在脑出血继发性损伤中的作用及机制研究[D]. 重庆: 中国人民解放军陆军军医大学(第三军医大学), 2017.
MENG Zhaoyou. A20 Ameliorates Intracerebral Hemorrhage-Induced Inflammatory Injury by Regulating TRAF6 Polyubiquitination[D]. Chongqing: PLA Army Medical University (Third Military Medical University), 2017.

31. 张耀文. MicroRNA-132减轻脑出血模型小鼠的神经行为学及神经病理学改变[D]. 天津: 天津医科大学, 2017.
ZHANG Yaowen. MicroRNA-132 attenuates neurobehavioral and neuropathological changes associated with intracerebral hemorrhage in mice[D]. Tianjin: Tianjin Medical University, 2017.

32. 钱红, 刘理静, 谢明, 等. siRNA沉默EGFR表达减轻大鼠脑出血后脑损伤[J]. 基础医学与临床, 2016, 36(12): 1681-1686.
QIAN Hong, LIU Lijing, XIE Ming, et al. siRNA silencing EGFR expression alleviates brain injury stems from intracerebral hemorrhage of rats[J]. Basic & Clinical Medicine, 2016, 36(12): 1681-1686.

33. 杨慧, 万广, 高绚照, 等. Let-7a通过抑制MAP4K3/MKK4/JNK信号通路减少脑出血大鼠神经元凋亡[J]. 中国病理生理杂志, 2020, 36(6): 1055-1062.
YANG Hui, WAN Guang, GAO Xuanzhao, et al. let-7a inhibits MAP4K3/MKK4/JNK signaling pathway to decrease neuronal apoptosis in rats with intracerebral hemorrhage[J]. Chinese Journal of Pathophysiology, 2020, 36(6): 1055-1062.

本文引用：祁波, 冯凌云, 冒平. 微创血肿清除术后IL-6、GFAP、S100A8/A9水平与自发性脑出血患者功能预后的关系及其预测价值[J]. 临床与病理杂志, 2021, 41(11): 2580-2587. doi: 10.3978/j.issn.2095-6959.2021.11.014

Cite this article as: QI Bo, FENG Lingyun, MAO Ping. Relationship between IL-6, GFAP, S100A8/A9 levels and functional prognosis of patients with spontaneous intracerebral hemorrhage and their predictive value after minimally invasive evacuation of hematoma[J]. Journal of Clinical and Pathological Research, 2021, 41(11): 2580-2587. doi: 10.3978/j.issn.2095-6959.2021.11.014