

doi: 10.13241/j.cnki.pmb.2020.18.028

颅内介入栓塞术与颅内夹闭术对高分级动脉瘤性蛛网膜下腔出血患者神经功能、免疫状态及睡眠质量的影响*

孙 伟 黄冠敏 刘 园 路 飞 顾 锐

(安徽理工大学第一附属医院神经外科 安徽 淮南 232007)

摘要 目的:比较颅内介入栓塞术与颅内夹闭术对高分级动脉瘤性蛛网膜下腔出血(aSAH)患者神经功能、免疫状态及睡眠质量的影响。**方法:**回顾性分析我院自2015年1月到2019年8月收治的高分级aSAH患者80例的临床资料,根据手术方式的不同将患者分为A组(n=38,颅内夹闭术)和B组(n=42,颅内介入栓塞术),比较两组患者疗效、神经功能、免疫状态、睡眠质量及并发症发生情况。**结果:**B组的预后良好率为73.81%(31/42),高于A组的60.53%(23/38)($P<0.05$)。两组患者术后3个月美国国立卫生研究所卒中量表(NIHSS)、匹兹堡睡眠质量指数量表(PSQI)评分均降低,且B组低于A组($P<0.05$)。两组患者术后1d、术后5d免疫球蛋白(Ig)G、IgA及IgM均呈先下降后升高趋势,B组术后1d、术后5d IgG、IgA及IgM均高于A组($P<0.05$)。B组的术后并发症发生率为11.90%(5/42),低于A组的31.58%(12/38)($P<0.05$)。**结论:**颅内介入栓塞术应用于高分级aSAH患者的疗效优于颅内夹闭术,并且可以改善患者的神经功能、睡眠质量,减少并发症发生风险,减轻免疫抑制。

关键词:颅内介入栓塞术;颅内夹闭术;动脉瘤性蛛网膜下腔出血

中图分类号:R743.34 文献标识码:A 文章编号:1673-6273(2020)18-3524-04

Effects of Intracranial Interventional Embolization and Intracranial Clipping on Neurologic Function, Immune Status and Sleep Quality of Patients with High Grade Aneurysmal Subarachnoid Hemorrhage*

SUN Wei, HUANG Guan-min, LIU Yuan, LU Fei, GU Rui

(Department of Neurosurgery, The First Affiliated Hospital of Anhui University of Technology, Huainan, Anhui, 232007, China)

ABSTRACT Objective: To compare the effects of intracranial interventional embolization and intracranial clipping on neurological function, immune status and sleep quality in patients with high-grade aneurysmal subarachnoid hemorrhage (aSAH). **Methods:** The clinical data of 80 patients with high-grade aSAH who were admitted to our hospital from January 2015 to August 2019 were analyzed retrospectively. According to the different operation methods, the patients were divided into group A (n = 38, intracranial clipping) and group B (n = 42, intracranial interventional embolization). The curative effect, neurological function, immune status, sleep quality and complications of the two groups were compared. **Results:** The good prognosis rate of group B was 73.81% (31/42), which was higher than 60.53% (23/38) of group A ($P < 0.05$). The scores of national Institutes of Health Stroke Scale (NIHSS), pittsburgh sleep quality index (PSQI) in the two groups were decreased, and the group B was lower than that in group A ($P < 0.05$). The levels of immunoglobulin (Ig)G, IgA and IgM in group B were decreased first and then increased at 1d after operation, 5d after operation, IgG, IgA and IgM in group B were higher than those in group A at 1d after operation, 5d after operation ($P < 0.05$). The incidence of postoperative complications in group B was 11.90% (5/42), which was lower than 31.58% (12/38) in group A ($P < 0.05$). **Conclusion:** Intracranial interventional embolization is superior to intracranial clipping in the treatment of high-grade aSAH, and it can improve the neurological function, sleep quality, reduce the risk of complications and immune suppression.

Key words: Intracranial interventional embolization; Intracranial clipping; Aneurysmal subarachnoid hemorrhage

Chinese Library Classification(CLC):R743.34 **Document code:** A

Article ID: 1673-6273(2020)18-3524-04

前言

动脉瘤性蛛网膜下腔出血(aneurysmal subarachnoid hemorrhage, aSAH)是由颅内动脉瘤破裂引起,约占所有卒中的5%,但由其造成的病死率高达25%,是危害人类生命安全的重

要疾病类型^[1-3]。脑血管痉挛是aSAH较为常见且也是最严重的并发症,其能够引起受累动脉的供血区域出现缺血现象^[4,5]。高分级aSAH则是世界神经外科联盟(WFNS)分级为IV~V级的aSAH患者,此类患者病情较重,需谨慎治疗^[6,7]。现临床针对高分级aSAH的治疗多以手术为主,其中以颅内介入栓塞术^[8]与

* 基金项目:安徽省卫生计生委科研计划项目(2016qk1108);淮南市科技计划项目(2018B55)

作者简介:孙伟(1979-),男,本科,主治医师,研究方向:脑血管病, E-mail: 13866310202@139.com

(收稿日期:2020-02-03 接受日期:2020-02-28)

颅内夹闭术^[9]较为常见,但有关两种手术治疗方案的具体优劣尚存在一定的争议,鉴于此,本研究通过比较两种手术方案对高分级 aSAH 患者神经功能、免疫状态及睡眠质量的影响,现报道如下。

1 资料与方法

1.1 一般资料

回顾性分析我院自 2015 年 1 月到 2019 年 8 月收治的高分级 aSAH 患者 80 例的临床资料,纳入标准:(1)临床表现为剧烈头痛、颈项痛、恶心呕吐,随机意识丧失或昏迷不醒,经颅脑 CT 或数字减影血管造影检查显示为 aSAH;(2)WFNS 分级为 IV~V 级;(3)均符合手术指征者;(4)年龄 35~75 岁者。排除标准:(1)预计生存时间<6 个月者;(2)合并严重肝肾功能障碍者;(3)复发性动脉瘤二次治疗者;(4)合并传染性疾病者;(5)合并凝血功能障碍者;(6)术前已伴有脑积水者。根据手术方式的不同将患者分为 A 组(n=38, 颅内夹闭术)和 B 组(n=42, 颅内介入栓塞术),其中 A 组男 16 例,女 22 例,年龄 35~72 岁,平均(54.29±9.08)岁;WFNS 分级 IV 级 23 例,V 级 15 例;动脉瘤破裂位置:后交通动脉 9 例,前交通动脉 12 例,椎基底动脉 11 例,大脑中动脉 6 例。B 组男 18 例,女 24 例,年龄 36~75 岁,平均(53.71±9.16)岁;WFNS 分级 IV 级 21 例,V 级 21 例;动脉瘤破裂位置:后交通动脉 10 例,前交通动脉 14 例,椎基底动脉 12 例,大脑中动脉 6 例。两组一般资料对比未见统计学差异($P>0.05$)。此研究已通过我院伦理学委员会批准进行。

1.2 方法

两组患者均在入院 3d 内实施手术,所有手术均由本院同一组医师共同完成。A 组患者予以颅内夹闭术,具体操作如下:全麻,根据动脉瘤具体位置确定手术入路。将头皮各层切开并分离,打开硬脑膜,采用日本欧林巴斯公司生产的 CHA 型显微镜观察患者脑血管解剖位置,对瘤颈进行分离,选择 90~120 mg 罂粟碱(哈药集团生物工程有限公司,国药准字:H20080022,规格:30 mg)对大血管进行浸泡,术中给予止血处理,逐层关闭切口,术后密切监测患者生命体征。B 组患者予以颅内介入栓塞术,行弹簧圈栓塞和支架辅助栓塞,具体操作如下:接受支架辅助栓塞治疗的患者在治疗开始前口服阿司匹林(赤峰万泽药业股份有限公司,国药准字:H10940218,规格:

0.3 g)100~200 mg,手术时患者全麻,根据血管造影结果对动脉瘤直径进行测量,随后轻柔置入微导管,确认微导管位置,在预定位置放好弹簧圈后手术结束。术后给予尼莫地平(福建省闽东力捷迅药业有限公司,国药准字:H20060182,规格:4 mg)抗脑血管痉挛治疗,50 mg/次,2 次/d。患者维持 24h 以上的持续卧床。

1.3 观察指标

(1)术后两组患者采用门诊复查的方式随访 3 个月。采用格拉斯哥结局量表(Glasgow outcome scale, GOS)^[10]评价患者术后 3 个月的临床疗效。其中日常生活未见影响,症状、体征较轻为恢复良好;丧失部分生活、工作能力,但可自主活动,存在神经麻痹、共济失调等残疾为中度残疾;有一定意识,但无自主生活能力,伴有语言、感觉障碍为重度残疾;无意识,仅存眨眼、呼吸等局部动作为植物生存。预后良好率=恢复良好率+中度残疾率。(2)于术前、术后 3 个月采用美国国立卫生研究所卒中量表(National institutes of health stroke scale, NIHSS)^[11]评价两组患者神经功能,其中 NIHSS 量表含有 12 项内容,总分 42 分,分数越高,神经损伤越严重。(3)于术前、术后 1d、术后 5d 抽取患者肘静脉血 4 mL,经离心处理(离心半径 8 cm, 3800 r/min 离心 12 min)分离上清液,置于冰箱(-30℃)中待测。选用深圳晶美生物科技有限公司生产的试剂盒,采用免疫比浊法检测血清免疫球蛋白(Immunoglobulin, Ig)G、IgA 及 IgM 水平。(4)记录两组患者术后并发症发生情况,包括脑积水、颅内感染、脑血管痉挛、再出血等。(5)于术前、术后 3 个月采用匹兹堡睡眠质量指数量表(Pittsburgh sleep quality index, PSQI)^[12]评价患者的睡眠质量,其中 PSQI 量表包括睡眠障碍、日间功能、入睡时间、睡眠效率、催眠药物、睡眠时间、睡眠质量这 7 项,每一项 0~3 分,总分 21 分,分数越高睡眠质量越差。

1.4 统计学方法

通过 SPSS25.0 软件处理统计数据。计数资料用率表示,实施 χ^2 检验。计量资料用($\bar{x}\pm s$)表示,两组间实施 t 检验。检验水准 $\alpha=0.05$, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 临床疗效比较

B 组的预后良好率为 73.81%(31/42),高于 A 组的 60.53%(23/38),差异有统计学意义($P<0.05$);详见表 1。

表 1 两组临床疗效比较例(%)

Table 1 Comparison of clinical effects between the two groups n(%)

Groups	Recovered well	Moderate disability	Severe disability	Plant survival	Favorable prognosis
Group A(n=38)	7(18.42)	16(42.11)	11(28.95)	4(10.52)	23(60.53)
Group B(n=42)	12(28.57)	19(45.24)	8(19.05)	3(7.14)	31(73.81)
χ^2					4.067
P					0.044

2.2 两组患者神经功能、睡眠质量比较

两组患者术前 NIHSS、PSQI 评分比较差异无统计学意义($P>0.05$);两组患者术后 3 个月 NIHSS、PSQI 评分均降低,且 B 组低于 A 组($P<0.05$);详见表 2。

2.3 两组患者免疫状态比较

两组患者术前 IgG、IgM、IgA 比较差异无统计学意义($P>0.05$);两组患者术后 1d、术后 5d IgG、IgM、IgA 均呈先下降后升高趋势, B 组术后 1d、术后 5d IgG、IgM、IgA 均高于 A 组($P<0.05$);详见表 3。

05);详见表 3。

表 2 两组患者神经功能、睡眠质量比较($\bar{x}\pm s$,分)

Table 2 Comparison of neurological function and sleep quality between the two groups($\bar{x}\pm s$, score)

Groups	NIHSS		PSQI	
	Before operation	3 months after operation	Before operation	3 months after operation
Group A(n=38)	24.52±2.39	15.72±2.71 ^a	15.86±1.63	10.21±1.37 ^a
Group B(n=42)	24.28±2.56	10.27±1.64 ^a	15.37±1.47	5.69±1.15 ^a
t	0.432	11.000	1.414	16.034
P	0.667	0.000	0.161	0.000

Note: compared with before operation, ^aP<0.05.

表 3 两组患者免疫状态比较($\bar{x}\pm s$)

Table 3 Comparison of immune status between the two groups($\bar{x}\pm s$)

Groups	IgG(g/L)			IgM(g/L)			IgA(g/L)		
	Before operation	1d after operation	5d after operation	Before operation	1d after operation	5d after operation	Before operation	1d after operation	5d after operation
Group A (n=38)	12.27±1.25	7.28±1.20 ^a	10.91±1.35 ^{ab}	1.73±0.57	0.96±0.48 ^a	1.43±0.36 ^{ab}	2.51±0.49	1.54±0.32 ^a	2.16±0.29 ^{ab}
Group B (n=42)	12.41±1.32	9.14±1.25 ^a	11.68±1.79 ^b	1.78±0.44	1.34±0.32 ^a	1.67±0.45 ^b	2.46±0.35	1.96±0.31 ^a	2.38±0.34 ^b
t	0.486	6.773	2.154	0.441	4.202	2.616	0.529	5.959	3.097
P	0.628	0.000	0.034	0.660	0.000	0.011	0.598	0.000	0.003

Note: compared with before operation, ^aP<0.05; compared with 1d after operation, ^bP<0.05.

2.4 两组患者并发症发生率比较

31.58%(12/38)(P<0.05);详见表 4。

B 组的术后并发症发生率为 11.90%(5/42), 低于 A 组的

表 4 两组患者并发症发生率比较[例(%)]

Table 4 Comparison of the incidence of complications between the two groups [n(%)]

Groups	Hydrocephalus	Intracranial infection	Cerebral vasospasm	Rebleeding	Total incidence rate
Group A(n=38)	1(2.63)	3(7.89)	6(15.79)	2(5.26)	12(31.58)
Group B(n=42)	1(2.38)	1(2.38)	2(4.76)	1(2.38)	5(11.90)
χ^2					5.692
P					0.017

3 讨论

高分级 aSAH 患者病情危急,其死亡率和致残率在 50%以上,存在高死亡率和致残率的特点,预后较差^[13,14]。既往临床针对高分级 aSAH 患者多给予保守治疗,待患者分级降级后,再给予手术治疗^[15]。但近年来的临床实践证明此类治疗方案效果并不理想,故临床主张直接选择外科手术治疗^[16]。颅内夹闭术是临床治疗高分级 aSAH 患者较为传统的术式,可有效防止动脉瘤再次破裂,有效清除蛛网膜下腔积血和脑内血肿,但此术式解剖范围较大,术后创伤大,对血管造成的创伤也较重,极易引起神经损伤,同时还可影响患者后续睡眠质量,降低临床治疗效果^[17-19]。同时该术式对于较深部位的动脉瘤,手术空间受限,手术操作难度大^[20]。近年来,颅内介入栓塞术取得了较大的临床进展,颅内介入栓塞术可通过特殊的导管系统,借助高分辨率的显微镜进行手术,将弹簧圈置入动脉腔内并填满,在术

中不会造成脑损伤加重,可一次性处理多个动脉肿瘤,不会影响动脉瘤周围重要结构,已逐渐得到医学界的关注和认可^[21-23]。

本次研究结果显示,B 组的预后良好率高于 A 组,B 组术后 NIHSS、PSQI 评分低于 A 组,提示颅内介入栓塞术应用于高分级 aSAH 患者,神经功能缺损程度恢复状况较好,可有效促进患者睡眠质量改善,疗效显著。尽管颅内夹闭术可清晰显示局部蛛网膜下腔出血情况,但此类术式解剖范围较大,引发穿支动脉损伤的风险较高^[24,25]。颅内介入栓塞术利用弹簧圈在瘤腔中进行填塞,可减慢甚至阻断动脉瘤内血流速度,使瘤腔内血栓机化,进而瘤颈内膜化,从而达到治愈疾病的目的^[26,27]。同时颅内介入栓塞术符合微创外科的理念,患者术后神经功能恢复快,对于改善患者睡眠质量,后续生活质量具有积极意义^[28]。本次研究结果还显示,两种手术均可对机体免疫功能造成影响,其中颅内介入栓塞术的免疫抑制程度更轻,这可能是因为颅内夹闭术可对局部组织血管造成影响,进而影响机体内分泌

和免疫功能^[29],而颅内介入栓塞术可有效避免对局部组织血管造成的损伤,进而促进患者恢复。另外B组的术后并发症发生率低于A组,高分级aSAH术后常见并发症主要由化学、物理等刺激共同作用所致,其中化学刺激主要为内皮素、氧自由基等所致,而物理刺激则是术中手术器械对血管壁造成的损伤。颅内介入栓塞术治疗创伤小,不会引发较大出血,同时还可促进蛛网膜下腔积血的吸收,故并发症发生率明显减轻^[30]。值得注意的是,颅内介入栓塞术操作精细,对施术者具有一定的要求,需严格掌握手术操作及指征,以便获取更好的治疗效果。

综上所述,与颅内夹闭术相比,颅内介入栓塞术应用于高分级aSAH患者,在改善患者神经功能、睡眠质量、并发症发生率方面效果显著,同时还可减轻免疫抑制,疗效确切。

参考文献(References)

- [1] Lucke-Wold BP, Logsdon AF, Manoranjan B, et al. Aneurysmal Subarachnoid Hemorrhage and Neuroinflammation: A Comprehensive Review[J]. *Int J Mol Sci*, 2016, 17(4): 497
- [2] Garg R, Bar B. Systemic Complications Following Aneurysmal Subarachnoid Hemorrhage [J]. *Curr Neurol Neurosci Rep*, 2017, 17(1): 7
- [3] Pérez-Neri I, Diéguez-Campa CE. Taurine and aneurysmal subarachnoid hemorrhage prognosis[J]. *Postgrad Med*, 2018, 130(8): 669-672
- [4] Liu H, Xu X. Effect of simvastatin in patients with aneurysmal subarachnoid hemorrhage: A systematic review and meta-analysis[J]. *Am J Emerg Med*, 2017, 35(12): 1940-1945
- [5] Ohkuma H, Shimamura N, Naraoka M, et al. Aneurysmal Subarachnoid Hemorrhage in the Elderly over Age 75: A Systematic Review[J]. *Neurol Med Chir (Tokyo)*, 2017, 57(11): 575-583
- [6] Datar S, Rabinstein AA. Postinterventional critical care management of aneurysmal subarachnoid hemorrhage [J]. *Curr Opin Crit Care*, 2017, 23(2): 87-93
- [7] Karic T, Røe C, Nordenmark TH, et al. Effect of early mobilization and rehabilitation on complications in aneurysmal subarachnoid hemorrhage[J]. *J Neurosurg*, 2017, 126(2): 518-526
- [8] Trivelato FP, Abud DG, Ułhōa AC, et al. Derivo Embolization Device for the Treatment of Intracranial Aneurysms [J]. *Stroke*, 2019, 50(9): 2351-2358
- [9] Meling TR, Romundstad L, Niemi G, et al. Adenosine-assisted clipping of intracranial aneurysms[J]. *Neurosurg Rev*, 2018, 41(2): 585-592
- [10] 刘永昌, 李少泉, 李连生, 等. 颅内动脉瘤性蛛网膜下腔出血术后预后不良危险因素分析[J]. *医学临床研究*, 2016, 33(2): 229-231
- [11] 袁波, 谭莉, 李鑫, 等. 缺血性脑卒中 NIHSS 评分与卒中抑郁的相关性分析 [J]. *中国神经免疫学和神经病学杂志*, 2018, 25(6): 430-432, 461
- [12] 龚为群, 阎萍, 杨世权, 等. Epworth 嗜睡量表联合匹兹堡睡眠质量指数量表在不同程度鼻源性 OSAHS 患者中的临床应用 [J]. *重庆医学*, 2016, 45(32): 4549-4551
- [13] Lu AY, Damisah EC, Winkler EA, et al. Cerebrospinal fluid untargeted metabolomic profiling of aneurysmal subarachnoid hemorrhage: an exploratory study[J]. *Br J Neurosurg*, 2018, 32(6): 637-641
- [14] de Oliveira Manoel AL, Turkel-Parrella D, Duggal A, et al. Managing aneurysmal subarachnoid hemorrhage: It takes a team[J]. *Cleve Clin J Med*, 2015, 82(3): 177-192
- [15] Perez P, Lukaszewicz AC, Lenck S, et al. Platelet activation and aggregation after aneurysmal subarachnoid hemorrhage [J]. *BMC Neurol*, 2018, 18(1): 57
- [16] Mejdoubi M, Schertz M, Zanolli S, et al. Transoceanic Management and Treatment of Aneurysmal Subarachnoid Hemorrhage: A 10-Year Experience[J]. *Stroke*, 2018, 49(1): 127-132
- [17] Yang H, Jiang H, Ni W, et al. Treatment Strategy for Unruptured Intracranial Aneurysm in Elderly Patients: Coiling, Clipping, or Conservative?[J]. *Cell Transplant*, 2019, 28(6): 767-774
- [18] Campe C, Neumann J, Sandalcioğlu IE, et al. Vasospasm and delayed cerebral ischemia after uneventful clipping of an unruptured intracranial aneurysm - a case report [J]. *BMC Neurol*, 2019, 19(1): 226
- [19] Linzey JR, Wilkinson DA, Nadel JL, et al. Complications in Patients Undergoing Microsurgical Clipping of Intracranial Aneurysms with Pre-existing Ventriculoperitoneal Shunts Following a Cranial Procedure[J]. *J Stroke Cerebrovasc Dis*, 2019, 28(3): 845-849
- [20] Elgebaly AS, Abd El Ghafar MS, Fathy SM, et al. Vasopressin Continuous Infusion Improves Intracranial Pressure and Patient Outcomes after Surgical Clipping or Endovascular Coiling of Cerebral Aneurysm[J]. *Anesth Essays Res*, 2019, 13(3): 528-534
- [21] Volders D, Stapf C, Ghostine J, et al. Intracranial Embolization and Retrieval of a Sheared Coronary Artery Segment[J]. *JACC Cardiovasc Interv*, 2019, 12(7): e55-e57
- [22] Zou L, Hou Y, Yu B, et al. The effect of intravascular interventional embolization and craniotomy on MMP-2, MMP-9 and caspase3 in serum of intracranial aneurysm patients [J]. *Exp Ther Med*, 2018, 16(6): 4511-4518
- [23] Haffaf I, Clarençon F, Shotar E, et al. Medina embolization device for the treatment of intracranial aneurysms: 18 months' angiographic results[J]. *J Neurointerv Surg*, 2019, 11(5): 516-522
- [24] Pierot L, Bannery C, Batchinsky-Parrou V, et al. Clipping of recanalized intracerebral aneurysms initially treated by the Woven EndoBridge device[J]. *J Neurointerv Surg*, 2019, 11(8): 807-811
- [25] 肖刚, 车旭东, 彭彤, 等. 栓塞和夹闭治疗对颅内动脉瘤患者认知功能的影响[J]. *现代生物医学进展*, 2017, 17(23): 4498-4501, 4509
- [26] 杨涛, 杨新宇, 任新亮, 等. 同期介入栓塞联合显微外科手术治疗颅内复杂动静脉畸形患儿一例报告 [J]. *中国医师进修杂志*, 2019, 42(11): 1041-1043
- [27] Martínez-Galdámez M, Orlov K, Kadziolka K, et al. Safety and efficacy of intracranial aneurysm embolization using the "combined remodeling technique": low-profile stents delivered through double lumen balloons: a multicenter experience [J]. *Neuroradiology*, 2019, 61(9): 1067-1072
- [28] Kole MJ, Miller TR, Cannarsa G, et al. Pipeline embolization device diameter is an important factor determining the efficacy of flow diversion treatment of small intracranial saccular aneurysms [J]. *J Neurointerv Surg*, 2019, 11(10): 1004-1008
- [29] Musara A, Yamada Y, Takizawa K, et al. Anterior Temporal Approach and Clipping of a High-Riding Basilar Tip Aneurysm: Case Report and Review of the Surgical Technique [J]. *Asian J Neurosurg*, 2019, 14(4): 1283-1287
- [30] 方治军, 张东. 颅内动脉瘤介入栓塞术后二次复发的影响因素分析[J]. *中华解剖与临床杂志*, 2019, 24(4): 375-379