

动脉瘤性蛛网膜下腔出血后发生认知障碍危险因素分析

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【摘要】目的 探讨动脉瘤性蛛网膜下腔出血(aSAH)后发生认知障碍的危险因素。**方法** 选取 122 例 aSAH 患者为研究对象,其中术后 2 周简易精神状态量表评分 <27 分 98 例,为认知障碍组;30~27 分 24 例,为正常组。分析 aSAH 后认知障碍与患者临床特征的关系,采用 logistic 回归分析 aSAH 后认知障碍危险因素。**结果** 患者性别、年龄、动脉瘤位置与 aSAH 后认知障碍的发生均无关,差异均无统计学意义(均 $P>0.05$);而术前 CT-Fisher 分级、术前 Hunt-Hess 分级、诊断明确至手术时间、动脉瘤大小、治疗方式与 aSAH 后认知障碍的发生均有关,差异均有统计学意义(均 $P<0.05$)。logistic 回归分析结果显示,治疗方式($OR=10.562, 95\%CI: 1.803\sim61.875$)、术前 CT-Fisher 分级($OR=0.066, 95\%CI: 0.004\sim1.061$)是 aSAH 后发生认知障碍的独立影响因素。**结论** 动脉瘤开颅夹闭术、术前 CT-Fisher 分级高是 aSAH 后发生认知障碍的独立危险因素。

【关键词】 蛛网膜下腔出血 颅内动脉瘤 认知障碍 开颅夹闭 栓塞术

Risk factors of cognitive dysfunction in patients with aneurysm subarachnoid hemorrhage YU Xuebin, JIN Guoliang, HUANG Chunmin, et al. Department of Neurosurgery, Shaoxing People's Hospital, Shaoxing 312000, China

【Abstract】Objective To analyze the risk factors of cognitive dysfunction in patients with aneurysm subarachnoid hemorrhage(aSAH). **Methods** One hundred and twenty two patients with aSAH were enrolled, including 98 patients with cognitive impairment (MMSE score <27 , cognitive impairment group) and 24 patients with normal cognition (MMSE score 27~30, normal group). The relationship between cognitive dysfunction and clinical data after aSAH was analyzed. Logistic regression was used to analyze the risk factors of cognitive dysfunction after aSAH. **Results** There were no significant differences in sex, age and location of aneurysm between the two groups(all $P>0.05$). Preoperative CT-Fisher grade, preoperative Hunt-Hess grade, waiting time, aneurysm size and treatment modality were all related to cognitive impairment after aSAH. Logistic regression analysis showed that treatment modality ($OR=10.562, 95\%CI: 1.803\sim61.875$) and preoperative CT-Fisher grade ($OR=0.066, 95\%CI: 0.004\sim1.061$) were independent risk factors of cognitive impairment after aSAH. **Conclusion** Clipping of aneurysm and preoperative high CT-Fisher grade are associated with cognitive impairment of after aSAH.

【Key words】 Subarachnoid hemorrhage Intracranial aneurysm Cognitive dysfunction Surgical clipping Embolization

动脉瘤性蛛网膜下腔出血(aneurysmal subarachnoid hemorrhage, aSAH)引起的认知障碍发生率高、持续时间长,对患者正常生活及工作影响较大。本研究通过分析认知障碍发生的危险因素,了解 aSHA 后认知功能损害的症状并进行有效预防,以期降低该后遗症的发生率。

1 对象和方法

1.1 对象 选取 2015 年 7 月至 2017 年 12 月本院收治的 122 例 aSAH 患者为研究对象,其中男 37 例,女 85

例;年龄 25~65(56.52 ± 7.68)岁;前交通动脉瘤 45 例,后交通动脉瘤 49 例,大脑中动脉动脉瘤 20 例,后循环动脉瘤 8 例;Hunt-Hess 分级 I 级 25 例, II 级 97 例;CT-Fisher 分级 I 级 27 例, II 级 29 例, III 级 66 例。纳入标准:(1)经腰穿或头部 CT 检查证实颅内蛛网膜下腔出血,无外伤史;(2)经脑血管造影证实颅内动脉瘤;(3) Hunt-Hess 分级 I~II 级;(4)CT-Fisher 分级 I~III 级;(5)小学及以上文化程度;(6)发病前无认知障碍史;(7)术后无严重并发症,如脑积水、脑出血、大面积脑梗死等;(8)签署知情同意书。

1.2 方法 收集所有患者的性别、年龄、动脉瘤位置、术前 Hunt-Hess 分级、术前 CT-Fisher 分级、诊断明确至手术时间、动脉瘤大小、治疗方式、术后 2 周简易精神

DOI:10.12056/j.issn.1006-2785.2019.41.18.2018-2815

基金项目:浙江省医药卫生科技计划项目(2015RCB031)

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状态量表(MMSE)评分等资料。MMSE 评价:术后 2 周(早期)采用 MMSE 评价认知功能,内容包括定向能力、记忆力、注意力和计算能力、回忆能力、语言能力的测试,总分 30 分。按照北京协和医院的评分标准,得分 30~27 分为正常,<27 分为认知障碍。

1.3 统计学处理 应用 SPSS 15.0 统计软件。计量资料用 $\bar{x} \pm s$ 表示,组间比较采用两独立样本 t 检验;计数资料用率表示,组间比较采用 χ^2 检验。aSAH 后认知障碍危险因素分析采用 logistic 回归。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 aSAH 后认知障碍与患者临床特征的关系 122 例 aSAH 患者术后早期发生认知障碍 98 例(80.3%),正常 24 例(19.7%)。患者性别、年龄、动脉瘤位置与 aSAH 后

认知障碍的发生均无关,差异均无统计学意义(均 $P > 0.05$);而术前 CT-Fisher 分级、术前 Hunt-Hess 分级、诊断明确至手术时间、动脉瘤大小、治疗方式与 aSAH 后认知障碍的发生均有关,差异均有统计学意义(均 $P < 0.05$),见表 1。

2.2 aSAH 后认知障碍危险因素分析 将上述 $P < 0.05$ 的变量纳入 logistic 回归分析,结果发现治疗方式、术前 CT-Fisher 分级是 aSAH 后认知障碍的独立影响因素,其 OR 值及 95%CI 分别为 10.562(1.803~61.875)、0.066(0.004~1.061),见表 2。

3 讨论

影响 aSAH 后发生认知障碍的因素很多,如年龄、性别、文化程度、SAH 本身及其并发症、动脉瘤位置、血糖、术前 Hunt-Hess 分级、手术时间、动脉瘤大小、治疗

表 1 aSAH 后认知障碍与患者临床特征的关系

临床特征	<i>n</i>	认知障碍	认知正常	χ^2/t 值	<i>P</i> 值
性别[<i>n</i> (%)]					
男	37	28(75.7)	9(24.3)		
女	85	70(82.4)	15(17.6)	0.727	>0.05
年龄(岁)	122	56.97 ± 6.87	54.92 ± 10.59	1.167	>0.05
动脉瘤位置[<i>n</i> (%)]					
前交通及大脑前	55	47(85.5)	8(15.5)		
后交通	38	28(73.7)	10(36.3)	3.748	>0.05
大脑中动脉	21	18(85.7)	3(14.3)		
后循环	14	5(35.7)	9(64.3)		
术前 CT-Fisher 分级[<i>n</i> (%)]					
I 级	27	11(40.7)	16(59.3)		
II 级	29	26(89.7)	3(10.3)	34.484	<0.05
III 级	66	61(92.4)	5(7.6)		
术前 Hunt-Hess 分级[<i>n</i> (%)]					
I 级	25	9(36.0)	16(64.0)	33.060	<0.05
II 级	97	89(91.8)	8(8.2)		
诊断明确至手术时间(d)	122	2.08 ± 1.57	3.58 ± 2.28	-3.811	<0.05
动脉瘤大小(mm)	122	6.14 ± 4.10	8.32 ± 5.42	-2.180	<0.05
治疗方式[<i>n</i> (%)]					
开颅夹闭	42	40(95.2)	2(4.8)	9.011	<0.05
介入栓塞	80	58(72.5)	22(27.5)		

表 2 aSAH 后认知障碍危险因素分析

变量	<i>B</i>	<i>SE</i>	Wald χ^2 值	<i>P</i> 值	OR 值	95%CI
术前 CT-Fisher 分级	-2.712	1.414	3.679	0.049	0.066	0.004~1.061
术前 Hunt-Hess 分级	-0.368	0.708	0.270	0.603	0.692	0.173~2.773
手术等待时间	-0.053	0.172	0.095	0.757	0.948	0.676~1.329
动脉瘤大小	-0.012	0.058	0.046	0.831	0.988	0.882~1.106
治疗方式	2.357	0.902	6.830	0.009	10.562	1.803~61.875

方式等。本研究结果发现,患者术前 CT-Fisher 分级、术前 Hunt-Hess 分级、诊断明确至手术时间、动脉瘤大小、治疗方式与 aSAH 后认知障碍均有关,而性别、年龄、动脉瘤位置与 aSAH 后认知障碍均无关。进一步作 logistic 回归分析发现,治疗方式、术前 CT-Fisher 分级是 aSAH 后发生认知障碍的独立影响因素。

CT-Fisher 分级可反映患者蛛网膜下腔出血的严重程度。Bendel 等^[1]认为 aSAH 患者 CT-Fisher 分级与认知功能有关。Bonares 等^[2]观察未破裂动脉瘤患者术后认知功能,结果发现患者无远期认知障碍,这说明发生认知障碍的根本原因是蛛网膜下腔出血后导致的脑血管痉挛、迟发性脑缺血。Zaki 等^[3]、Buunk 等^[4]深入研究发现,治疗 SAH 和动脉瘤后,由于脑灌注下降和脑血流的阻断,导致神经元之间联系的中断和神经网络的不同步、神经元的兴奋毒性和微型 RNA 变异,因此有相当比例的患者存在不同程度的神经、心理方面的损害,存在记忆力、注意力、意识活动速度、语言流畅性、工作能力等方面的认知障碍。本研究结果发现,术前 CT-Fisher 分级较高的 aSAH 患者存在的认知障碍更严重,同时 CT-Fisher 分级也是 aSAH 后发生认知障碍的独立影响因素。

Latimer 等^[5]回顾性研究发现,采取血管内栓塞术治疗颅内破裂动脉瘤的患者认知功能缺失明显少于开颅夹闭组,而夹闭组患者认知功能缺失主要缘于手术损伤;但是不管夹闭术还是栓塞术,都会导致患者长期的心理残疾和认知障碍,降低其生活质量,引起持续性焦虑。Escartin 等^[6]、Vieira 等^[7]研究认为,开颅动脉瘤夹闭术后患者认知障碍发生率明显高于栓塞术。但 Mukerji 等^[8]研究认为,两种手术方法对 aSAH 患者认知障碍的影响无明显差异。本研究手术团队的医生既能进行开颅夹闭,又能介入栓塞,而且夹闭与介入栓塞均有统一、标准的操作流程,尽量避免因术者经验对结果造成的影响。本研究结果发现,手术方式是 aSAH 后认知障碍的独立影响因素,开颅夹闭对患者认知功能的影响明显。笔者分析原因,可能与开颅夹闭术中对脑组织的牵拉、对部分穿支血管造成损伤、术中血管临时阻断等因素有关。Su 等^[9]、Ali 等^[10]利用 MRI 检查分析 aSAH 患者的影像学改变,结果发现外科组患者灰质萎缩更明显,主要在额底皮层与外科手术同侧的海马旁回,这可能是开颅夹闭组患者认知障碍发生率更高的原因。Haug 等^[11]比较前交通动脉瘤与大脑中动脉动脉瘤患者术后认知功能,认为前交通动脉瘤患者发生认知障碍的概率明显较高。但 Sheldon 等^[12]、Perea 等^[13]研究表明,工作记忆缺失

在 aSAH 患者中广泛存在,但不受动脉瘤位置的影响。而本研究也发现动脉瘤位置与 aSAH 后认知障碍无关,因此笔者认为可能与本组血管内治疗患者更多、开颅夹闭术的手法及熟练程度等有关。

综上所述,动脉瘤开颅夹闭术、术前 CT-Fisher 分级高是 aSAH 后发生认知障碍的独立危险因素。

4 参考文献

- [1] Bendel P, Koivisto T, Niskanen E, et al. Brain atrophy and neuropsychological outcome after treatment of ruptured anterior cerebral artery aneurysms: a voxel-based morphometric study [J]. *Neuroradiology*, 2009,51(11):711-722. DOI:10.1007/s00234-009-0552-5.
- [2] Bonares MJ, Egeto P, de Oliveira MAL, et al. Unruptured intracranial aneurysm treatment effects on cognitive function: a meta-analysis[J]. *J Neurosurg*, 2016, 124(3):784-790. DOI:10.3171/2014.12.JNS141625.
- [3] Zaki GMG, Srinivasan VM, Wagner K, et al. Cognitive sequelae of subarachnoid hemorrhage, cerebral aneurysm treatment, and neuropsychological assessment[J]. *World Neurosurg*, 2018, 18: 394-399. DOI:10.1016/j.wneu.2018.06.178.
- [4] Buunk AM, Spikman JM, Veenstra WS, et al. Social cognition impairments after aneurysmal subarachnoid haemorrhage: Associations with deficits in interpersonal behaviour, apathy and impaired self-awareness[J]. *Neuropsychologia*, 2017, 103:131-139. DOI:10.1016/j.neuropsychologia.2017.07.015.
- [5] Latimer SF, Wilson FC, McCusker CG, et al. Subarachnoid haemorrhage(SAH): long-term cognitive outcome in patients treated with surgical clipping or endovascular coiling[J]. *Disabil Rehabil*, 2013,35(10):845-850. DOI:10.3109/09638288.2012.709909.
- [6] Escartin G, Junqué C, Juncadella M, et al. Decision-making impairment on the Iowa Gambling Task after endovascular coiling or neurosurgical clipping for ruptured anterior communicating artery aneurysm[J]. *Neuropsychology*, 2012,26(2):172-180. DOI:10.1037/a0024336.
- [7] Vieira AC, Azevedo-Filho HR, Andrade G, et al. Cognitive changes in patients with aneurysmal subarachnoid hemorrhage before and early posttreatment: differences between surgical and endovascular[J]. *World Neurosurg*, 2012,78(1-2):95-100. DOI:10.1016/j.wneu.2011.09.021.
- [8] Mukerji N, Holliman D, Baisch S, et al. Neuropsychologic impact of treatment modalities in subarachnoid hemorrhage: clipping is no different from coiling[J]. *World Neurosurg*, 2010,74(1):129-138. DOI:10.1016/j.wneu.2010.05.009.
- [9] Su JB, E TZ, Guo QH, et al. Memory Deficits After Aneurysmal Subarachnoid Hemorrhage: A Functional Magnetic Resonance Imaging Study[J]. *World Neurosurg*, 2018,111:e500-e506. DOI:10.1016/j.wneu.2017.12.102.
- [10] Ali A, Tanirgan G, Sabanci PA, et al. Relation of gray-white

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综上所述,首次 DSA 阴性 sSAH 患者大部分预后良好,但复查 DSA 阳性率偏高。尤其对于非 PM-SAH 患者,实施二次 DSA 是有必要的。

4 参考文献

- [1] Alen JF, Lagares A, Lobato RD, et al. Comparison between perimesencephalic nonaneurysmal subarachnoid hemorrhage and subarachnoid hemorrhage caused by posterior circulation aneurysms[J]. *J Neurosurg*, 2003, 98(3):529–535. DOI:10.3171/jns.2003.98.3.0529.
- [2] Beseoglu K, Pannes S, Steiger, HJ, et al. Long-term outcome and quality of life after nonaneurysmal subarachnoid hemorrhage [J]. *Acta Neurochir (Wien)*, 2010, 152(3):409–416. DOI:10.1007/s00701-009-0518-8.
- [3] Konczalla J, Kashefiolasi S, Brawanski N, et al. Increasing numbers of nonaneurysmal subarachnoid hemorrhage in the last 15 years: antithrombotic medication as reason and prognostic factor? [J]. *J Neurosurg*, 2016, 124(6):1731–1737. DOI:10.3171/2015.5.JNS15161.
- [4] Connolly BJ, Pearce LA, Hart RG. Vitamin K antagonists and risk of subdural hematoma: meta-analysis of randomized clinical trials[J]. *Stroke*, 2014, 45(6):1672–1678. DOI:10.1161/STROKEAHA.114.005430.
- [5] Connolly BJ, Pearce LA, Kurth T, et al. Aspirin therapy and risk of subdural hematoma: meta-analysis of randomized clinical trials [J]. *J Stroke Cerebrovasc Dis*, 2013, 22(4):444–448. DOI:10.1016/j.jstrokecerebrovasdis.2013.01.007.
- [6] Van Calenbergh F, Plets C, Goffin J, et al. Nonaneurysmal subarachnoid hemorrhage: prevalence of perimesencephalic hemorrhage in a consecutive series[J]. *Surg Neurol*, 1993, 39(4):320–323.
- [7] Konczalla J, Platz J, Schuss P, et al. Non-aneurysmal non-traumatic subarachnoid hemorrhage: patient characteristics, clinical outcome and prognostic factors based on a single-center experience in 125 patients[J]. *BMC Neurol*, 2014, 14:140. DOI:10.1186/1471-2377-14-140.
- [8] Pathirana N, Refsum SE, McKinsty CS, et al. The value of repeat cerebral angiography in subarachnoid haemorrhage[J]. *Br J Neurosurg*, 1994, 8(2):141–146. DOI:10.3109/02688699409027960.
- [9] Boswell S, Thorell W, Gogela S, et al. Angiogram-negative subarachnoid hemorrhage: outcomes data and review of the literature [J]. *J Stroke Cerebrovasc Dis*, 2013, 22(6):750–757. DOI:10.1016/j.jstrokecerebrovasdis.2012.02.001.
- [10] Gupta SK, Gupta R, Khosla VK, et al. Nonaneurysmal nonperimesencephalic subarachnoid hemorrhage: is it a benign entity? [J]. *Surg Neurol*, 2009, 71(5):566–571. DOI:10.1016/j.surneu.2008.04.021.
- [11] Jung JY, Kim YB, Lee JW, et al. Spontaneous subarachnoid haemorrhage with negative initial angiography: a review of 143 cases[J]. *J Clin Neurosci*, 2006, 13(10):1011–1017. DOI:10.1016/j.jocn.2005.09.007.
- [12] Zuccoli G, Nardone R, Rajan D, et al. Nonaneurysmal Subarachnoid Hemorrhage in Sickle Cell Disease: Description of a Case and a Review of the Literature[J]. *Neurologist*, 2018, 23(4):122–127. DOI:10.1097/NRL.0000000000000181.
- [13] Amer RR, Bakhsh EA. Nonaneurysmal Perimesencephalic Subarachnoid Hemorrhage as an Atypical Initial Presentation of Cerebral Venous Sinus Thrombosis: A Case Report[J]. *Am J Case Rep*, 2018, 19(4):72–77.
- [14] Hasan TF, Duarte W, Akinduro OO, et al. Nonaneurysmal 'Pseudo-Subarachnoid Hemorrhage' Computed Tomography Patterns: Challenges in an Acute Decision-Making Heuristics [J]. *J Stroke Cerebrovasc Dis*, 2018, 27(9):2319–2326. DOI:10.1016/j.jstrokecerebrovasdis.2018.04.016.
- [15] Wu X, Liu R, Malhotra A. Concerning 'Nonaneurysmal Perimesencephalic Hemorrhage Is Associated with Deep Cerebral Venous Drainage Anomalies: A Systematic Literature Review and Meta-Analysis'[J]. *Am J Neuroradiol*, 2017, 38(2):E14. DOI:10.3174/ajnr.A4984.
- [16] Rouchaud A, Lehman VT, Murad MH, et al. Nonaneurysmal Perimesencephalic Hemorrhage Is Associated with Deep Cerebral Venous Drainage Anomalies: A Systematic Literature Review and Meta-Analysis[J]. *Am J Neuroradiol*, 2016, 37(9):1657–1663. DOI:10.3174/ajnr.A4806.

(收稿日期:2019-05-30)

(本文编辑:陈丹)

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- matter ratio with long-term cognitive functions and quality of life in patients with mild to moderate aneurysmal subarachnoid hemorrhage: a prospective observational study[J]. *Acta Neurochir (Wien)*, 2018, 160(1):181–189. DOI:10.1007/s00701-017-3374-y.
- [11] Haug T, Sorteberg A, Sorteberg W, et al. Cognitive functioning and health related quality of life after rupture of an aneurysm on the anterior communicating artery versus middle cerebral artery [J]. *Br J Neurosurg*, 2009, 23(5):507–515. DOI:10.1080/02688690902785701.

- [12] Sheldon S, Macdonald RL, Cusimano M, et al. Long-term consequences of subarachnoid hemorrhage: examining working memory[J]. *J Neurol Sci*, 2013, 332(1–2):145–147. DOI:10.1016/j.jns.2013.06.021.
- [13] Perea BMV, Ladera FV, Maíllo SA. Long-term cognitive deficits in patients operated on for cerebral aneurysm by craniotomy and clipping[J]. *Neurologia*, 2009, 24(6):379–385.

(收稿日期:2018-11-15)

(本文编辑:陈丹)