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## 基于卒中登记的颅内动脉瘤致蛛网膜下腔出血的临床研究\*

刘会 荣良群<sup>△</sup> 魏秀娥 朱本亮 杨森 袁勇 王兰琴

(徐州医学院第二附属医院神经内科 江苏 徐州 221006)

**摘要 目的:**研究基于卒中登记的颅内动脉瘤致蛛网膜下腔出血(aneurysmal subarachnoid hemorrhage, aSAH)的颅脑血流动力学改变及其对诊断治疗的指导作用。**方法:**采用回顾性研究经卒中登记系统筛选出48例经DSA(digital subtraction angiography, DSA)确诊的aSAH,收集患者床旁经颅多普勒(transcranial Doppler, TCD)监测大脑中动脉(middle cerebral artery, MCA)的动脉平均峰值流速(mean blood velocity, Vm)、搏动指数(pulsatility index, PI)、阻力指数(resistance index, RI),自身健侧作为正常对照,均采用血管内介入治疗,对其中符合脑血管痉挛(cerebral vasospasm, CVS)诊断标准的患者使用尼莫地平进行治疗,观察疗效。**结果:**与健侧相比,患侧PI、RI增大,Vd、Vm减小,其中以Vd减小较明显,与健侧相比有统计学差异( $P < 0.01$ ),Vs与健侧相比无统计学差异( $P > 0.05$ )。CVS组与非CVS组相比Vm明显增加,有统计学差异( $P < 0.001$ )。所有患者经水膨胀弹簧圈或支架预后均得到改善。**结论:**床旁实时TCD监测能反映aSAH脑血流变化,对CVS进行及时解除痉挛治疗,并为介入治疗提供参考依据,颅脑血流实时监测和介入治疗综合运用提高了aSAH患者的治疗效果。

**关键词:**蛛网膜下腔出血;颅内动脉瘤;卒中登记;经颅多普勒超声;脑血管痉挛

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## Clinical Research on Aneurysmal Subarachnoid Hemorrhage Based on Stroke Registry\*

LIU Hui, RONG Liang-qun<sup>△</sup>, WEI Xiu-e, ZHU Ben-liang, YANG Sen, YUAN Yong, WANG Lan-qin

(Department of Neurology, the Second Affiliated Hospital of Xuzhou Medical College, Xuzhou, Jiangsu, 221006, China)

**ABSTRACT Objective:** To study the brain blood flow change and its benefit for the diagnosis and treatment of aneurysmal subarachnoid hemorrhage (aSAH) based on stroke registry. **Methods:** A retrospective single center method based on stroke registry was applied in this study and 48 patients' clinical data with aSAH diagnosed by digital subtraction angiography (DSA) were registered, which contained transcranial Doppler (TCD) parameters including the mean blood velocity (Vm), pulsatility index (PI), and resistance index (RI) of the middle cerebral artery (MCA), with a control of self healthy side. All patients were treated with interventional therapy and the results were collected and analyzed, in which there were some cerebral vasospasm (CVS) detected and treated with Nimodipine. **Results:** The data of TCD show that PI and RI were increased, and Vd and Vm decreased, in which there were statistical significance in PI, RI, Vd and Vm between ill side and healthy side ( $P < 0.01$ ). And there were no statistical significance in Vs ( $P > 0.05$ ). There were statistical differences in Vm between CVS group and non CVS group,  $P < 0.001$ . All the patients were relieved by interventional therapy with the water expansion spring coil or stents. **Conclusion:** The parameters of TCD could reflect the changes of brain blood flow, which were helpful for the diagnosis and treatment of aSAH. And it is also helpful for the personalized treatment of CVS detected by TCD and for the decrease of lethality and disability of aSAH.

**Key words:** Subarachnoid hemorrhage; Aneurysm; Stroke registry; Transcranial Doppler; Cerebral vasospasm

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### 前言

颅内动脉瘤是颅内动脉血管由于先天异常或者后天损伤等因素导致局部的血管壁损害,在血流动力学和其他因素作用下,逐渐扩张形成的异常膨出。研究表明,颅内动脉瘤的发生与吸烟、酗酒、高血压、性别等因素有关<sup>[1]</sup>。蛛网膜下腔出血(subarachnoid hemorrhage, SAH)指脑底部或脑表面的血管破裂,血液直接流入蛛网膜下腔引起的一种临床综合征,是一种非常严重的常见疾病<sup>[2]</sup>。根据患者脑灌注情况对血压进行科学的监测

和管理,改善SAH预后,加强病情监测一直是研究的热点<sup>[3-5]</sup>。而颅内动脉瘤致蛛网膜下腔出血(aneurysmal subarachnoid hemorrhage, aSAH)的临床表现较典型,但是每个患者表现可能不一<sup>[6]</sup>。aSAH发生后3d内行CT检查的敏感性很高(接近100%),但此后几天逐渐下降,5~7天后CT检查假阴性率急剧增加<sup>[7]</sup>。经颅多普勒(transcranial doppler, TCD)超声技术是目前颅内血流动力学检查中能反映脑血管内血流动力学的有效手段<sup>[8,9]</sup>。但是,目前关于TCD应用于aSAH脑血流监测及其诊治应用尚无统一标准,我们采用回顾性研究对卒中登记系统

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作者简介:刘会(1982-),女,硕士,主治医师,主要研究方向:脑血管病诊治,E-mail:liuhui2014tg@163.com,电话:13685112764

<sup>△</sup>通讯作者:荣良群(1962-),电话:0516-85326234,E-mail:rongliangqun@163.com

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筛选经 DSA (digital subtraction angiography, DSA) 确诊的 aSAH 患者大脑中动脉(middle cerebral artery, MCA)TCD 检测结果、脑血管痉挛(cerebral vasospasm, CVS)发生率及介入治疗结果进行分析,结果如下。

## 1 临床资料

### 1.1 病例登记方法

采用卒中注册软件<sup>[9]</sup>,回顾性研究经连续登记的徐州医学院第二附属医院神经内科 2010 年 1 月~2013 年 6 月收治的所有首次发病且发病 14 d 以内的 aSAH 患者的临床资料。病例入选标准:(1)符合 1995 年第四届全国脑血管学术会议制订的脑血管病 aSAH 诊断标准且经 DSA 确诊<sup>[10]</sup>;(2)单侧发生 aSAH;(3)脑血管事件发生的时间距就诊时间 < 14 d;(4)年龄 > 18 岁,文化程度小学以上;(5)在徐州地区居住 2 y 以上;(6)既往无卒中病史。排除标准:(1)无症状及体征的静止性梗死;(2)非脑血管事件;(3)发病至就诊的时间 > 14 d;(4)既往有卒中病史;(5)无 TCD 监测数据;(6)合并严重心、肺、肝、肾及血液系统疾病;(7)合并严重白内障、青光眼、视神经萎缩等明显影响视力者。

### 1.2 主要方法

我科采用德国 DWL 公司经颅多普勒系统进行监测,血压由动态血压监测仪由护师专职管理记录,全部患者均经 DSA 检查确诊,均在入院后即行床旁 TCD 监测并同时行腰穿脑脊液压力测量脑压,结果脑脊液初始压力均  $\geq 200$  mmH<sub>2</sub>O。患者取仰卧位,将 2MHz 脉冲探头垂直至于颞窗处监测患侧 MCA

的血流速度,取样层厚为 10 mm,超声功率 50 mW/cm,取样深度为 50~55 mm,调整方向,直接获得最佳的多普勒信号为止,显示收缩期峰值血流速度(Vs),舒张末期峰值血流速度(Vd),平均血流速度(Vm),搏动指数(PI),阻力指数(RI),由 1 名富有经验的医师操作确认。其中,aSAH 导致 CVS 诊断采用华扬标准<sup>[2]</sup>,血流速度的正常值采用高山等标准<sup>[13]</sup>。介入治疗预后根据格拉斯哥预后评分(GOS)判定。

### 1.3 统计学分析

计量资料以  $\bar{x} \pm s$  表示,计量资料两两比较运用两样本 t 检验,等级资料两两比较运用两个独立样本比较的 Wilcoxon 秩和检验,采用 PASW Statistics 18 统计软件分析,P < 0.05 为有统计学意义。

## 2 结果

### 2.1 一般资料

共收集符合上述入选标准和排除标准的观察对象共 48 例,其中男 28 例,女 20 例,年龄 40~76 岁,平均年龄  $52 \pm 8$  岁。患者中有出现嗜睡、昏睡和昏迷等意识障碍,有头痛、恶心、呕吐和眼底有视神经乳头水肿,伴有或无高血压或心动过缓,其中格拉斯哥昏迷量表(GCS)评分为 3~5 分者 14 例,6~8 分者 21 例,9~15 分者 13 例,选择健侧为对照组。

### 2.2 TCD 参数的变化

TCD 监测 aSAH 患者患侧和健侧 MCA 血流动力学,各指标结果见表 1。由表 1 可以看出,与健侧相比,患侧 PI、RI 增大,Vd、Vm 减小,其中以 Vd 减小较明显,与健侧相比有统计学差异(P < 0.01),Vs 与健侧相比无统计学差异(P > 0.05)。

表 1 aSAH 患侧与健侧 TCD 监测各参数比较(n=48,  $\bar{x} \pm s$ , cm/s)

Table 1 Comparison of TCD parameters between ill and healthy side of aSAH patients (n=48,  $\bar{x} \pm s$ , cm/s)

Groups	Vs	Vd	Vm	PI	RI
Ill side	79.02± 22.53	25.31± 9.96	43.49± 11.86	1.71± 0.72	0.77± 0.12
Healthy side	84.88± 9.43	41.18± 9.03	59.08± 9.73	0.81± 0.16	0.59± 0.14
t	1.405	7.546	6.353	6.442	4.943
P value	0.171	<0.001	<0.001	<0.001	<0.001

### 2.3 CVS 检出结果

参考文献 12 中 CVS 分级,本组病例按照此分级标准检查结果见表 2。将发病后 1d,3d,7d 的 CVS 组与 CVS 组 Vm 进行比较,CVS 组 MCA 血流速度伤后即呈进行性升高,出血第 3~

5 d 达高峰,随后逐渐回落但仍明显高于正常值;而非 CVS 组 MCA Vs 伤后 3 d 内维持正常范围,出血 5 d 略有升高,随后回落接近正常。非 CVS 组与 CVS 组 Vm 比较,有统计学差异,P < 0.001,见表 2。

表 2 CVS 组与非 CVS 组出血后 Vm 比较(n=48,  $\bar{x} \pm s$ , cm/s)

Table 2 Comparison of Vm between CVS and non-CVS groups (n=48,  $\bar{x} \pm s$ , cm/s)

Groups	1d	3d	5d	7d
CVS group(19)	75.8± 23.9	147.9± 27.8	141.4± 18.9	100.5± 22.2
non-CVS group(29)	55.1± 14.1	59.2± 25.6	75.8± 17.9	74.7± 20.8
t	3.98	13.0	13.9	4.67
P value	<0.001	<0.001	<0.001	<0.001

### 2.4 aSAH 介入治疗结果

本组 48 例 aSAH 患者均行介入治疗,所有患者出院前均复查头颅 CT,出院后随访 8-24 月,CVS 组与非 CVS 组患者预

后按格拉斯哥预后评分(Glasgow outcome scale, GOS)统计,结果表明两组比较无统计学差异,P > 0.05。

表 3 CVS 组与非 CVS 组 GOS 比较(n=48)

Table 3 Comparison of GOS between CVS and non-CVS groups (n=48)

Groups	Good recovery	Moderate disability	Severe disability	Vegetative state	Dead	P value
CVS group(19)	6	5	5	1	2	0.784
non-CVS group(29)	10	8	7	1	3	

### 3 讨论

颅内动脉瘤一旦破裂出血,致死致残率极高,对于有手术适应症的颅内动脉瘤应积极干预<sup>[4]</sup>。目前手术治疗方法主要有开颅夹闭和血管内介入治疗,而且目前国际大规模临床 aSAH 试验结果表明,介入治疗比开颅夹闭能够降低致死率,改善临床预后<sup>[5]</sup>。本组基于卒中系统注册的病例均采用的是介入治疗。

TCD 是一项检测颅内大动脉近段血流速度和方向的无创性超声技术,需要有一定培训和经验的操作者来实施操作并解释检测结果,且能连续监测,可床旁操作,已经广泛用于重症患者的床旁监测和疗效观察<sup>[6]</sup>。TCD 监测包括血流速度参数和频谱两部分,其血流速度参数指标如 Vd、Vs、Vm、PI、RI 比频谱更为有临床价值<sup>[7]</sup>;PI 主要反映脑血管阻力的变化,Vm 主要受收缩压的影响,脑血管阻力又取决于脑血管直径和 ICP,因此这些参数可反映脑血流动力学的变化。MCA 是颈内动脉的直接延伸部分,系供应大脑半球最粗大的动脉,其供应大脑半球所需血流量的 80%左右<sup>[8]</sup>,可基本上反映颈内动脉幕上血流情况,所以本组患者注册系统设计时选择 MCA 为颅内血流监测对象。

TCD 结果显示,患侧 Vd、Vm 与健侧相比有统计学差异( $P < 0.01$ ),Vs 与健侧相比无统计学差异( $P > 0.05$ )。PI、RI 与对照组相比有统计学差异( $P < 0.01$ ),PI、RI 和血流速度更能反映 ICP 的变化,当  $PI > 1.0$ , $RI > 0.6$  时,应考虑 ICP 升高。ICP 升高时 TCD 血流频谱具有典型性,并可同时作为监测 ICP 的重要指标。当脑血流自动调节功能存在时,随 ICP 增高, CPP 减少,为了保持 CPP 的恒定,势必导致脑小动脉扩张及外周阻力减少,而外周阻力减少时,其舒张压下降比收缩压的下降更明显,脉压差增大。由此可见 PI、RI 的增加提示 ICP 升高。此外,对 aSAH 患者患侧与健侧 PI 进行连续监测,其结果也显示出出血后 3d、7d 和 21d 患侧 PI 测量值较健侧明显升高,说明 SAH 发生后颅内血流灌注失代偿,ICP 明显升高。

CVS 为 aSAH 后脑动脉的迟发性收缩和狭窄,同时会引起相应部位脑组织血流量减少,重度和弥散性的 CVS 会导致局部脑血流量严重下降,从而出现神经功能缺损,是 aSAH 后的一种严重的并发症<sup>[9]</sup>,aSAH 后有高达 17%~40% 的患者因 CVS 出现迟发性缺血性神经功能障碍<sup>[10]</sup>,本组患者出现 CVS 占到 39.58%。目前认为,CVS 发病机制为,当细胞内钙离子浓度升高到一定水平时平滑肌即发生收缩,导致血管痉挛<sup>[11]</sup>,临床上常用钙通道阻滞剂尼莫地平防治 aSAH 后 CVS,以前对于所有 aSAH 患者是否使用尼莫地平尚无统一标准。本组患者经过 TCD 对脑血流进行监测,诊断为 aSAH 后 CVS 52 例,经尼莫地平治疗均得到缓解。最新的颅内动脉瘤血管内介入治疗中国专家共识中推荐<sup>[7]</sup>:(1)aSAH 后 CVS 发生率高,处理破裂动脉瘤后,引流蛛网膜下腔积血并启动尼莫地平治疗是预防 aSAH 后 CVS 的有效手段,尼莫地平的应用应该遵循“早期、足量、足程”的使用原则;(2)症状性 CVS 药物治疗无效或者 CVS 期间 aSAH 患者突然出现神经功能缺损,推荐行脑血管造影检查和(或)血管内介入治疗,包括球囊成形术或(和)动脉内抗痉挛药物灌注术。

本组患者 CVS 组与非 CVS 组介入治疗后 GOS 评分比较无统计学差异, $P > 0.05$ ,说明 CVS 组患者经过 TCD 检出后,采取尼莫地平治疗解除血管痉挛,恢复血流速度,使其治疗预后与非 CVS 组对比无统计学差异,明显降低了 CVS 患者致死

致残的可能性。TCD 床旁实时监测能反映颅内血流动力学的变化,随时预警 CVS 出现的可能性,给 aSAH 的治疗保驾护航,还能通过 PI 值预测脑出血 6 月后的预后恢复情况<sup>[12]</sup>。

本组病例经我院基于卒中注册系统按照入排标准筛选的,均有详实的入院诊断治疗以及随访资料,给卒中患者建立病例资料系统,不仅方便患者治疗,更有助于疾病的临床研究。本研究通过床旁 TCD 连续监测来观察 aSAH 患者颅内血流和 ICP 的变化,及时采取有效措施,同时还可用于评价治疗效果及判断预后。最新的 aSAH 治疗指南建议尽早启动尼莫地平治疗是预防 aSAH 后 CVS 的有效手段,本组病例也证实经 TCD 检出的 CVS 经过尼莫地平治疗后与非 CVS 组治疗预后无统计学差异。血管内介入治疗 aSAH 治疗有效,且治疗预后优于开颅夹闭。随着颅内动脉瘤血管内介入治疗治疗共识的制定,以及对于其资质认证的规范化,相信 aSAH 治疗能获得预期的治疗效果。

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