

成人烟雾病脑血管搭桥术后短期神经功能和临床症状改善单中心研究

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【摘要】 目的 对比分析不同发病类型和不同术式烟雾病患者脑血管搭桥术后短期预后。方法 纳入2010年1月至2011年10月首都医科大学附属北京天坛医院收治的44例烟雾病患者,均行脑血管搭桥术,术后3个月采用美国国立卫生研究院卒中量表(NIHSS)评估神经功能改善并观察临床症状改善,DSA或CTA判断桥血管是否通畅,记录手术相关并发症。结果 术后3个月,桥血管均保持通畅,无一例发生手术相关并发症。根据发病类型分为缺血型、出血型和混合型3组,缺血型患者术后3个月神经功能($\chi^2 = 3.853, P = 0.000$; $\chi^2 = 4.110, P = 0.000$)和临床症状($\chi^2 = 3.934, P = 0.000$; $\chi^2 = 4.138, P = 0.000$)改善情况优于出血型和混合型患者。根据术式分为前-额搭桥术、前-颞搭桥术、后-额搭桥术和后-颞搭桥术4组,行前-额搭桥术的患者神经功能改善情况优于前-颞搭桥术($\chi^2 = 2.079, P = 0.038$),行后-额搭桥术的患者神经功能和临床症状改善情况分别优于前-颞搭桥术($\chi^2 = 2.909, P = 0.004$; $\chi^2 = 2.812, P = 0.005$)和后-颞搭桥术($\chi^2 = 2.295, P = 0.022$; $\chi^2 = 2.580, P = 0.010$)。结论 缺血型烟雾病患者术后短期预后优于出血型和混合型患者,且行前-额搭桥术和后-额搭桥术的患者术后短期预后优于前-颞搭桥术和后-颞搭桥术。

【关键词】 脑底异常血管网病; 脑血管重建术; 颞动脉; 大脑中动脉; 预后

Short-term neurological function and clinical symptom improvement after cerebral revascularization in adults with moyamoya disease: a single-center study

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【Abstract】 Objective In this study, short-term prognosis of cerebral revascularization was evaluated by comparative analysis of patients with moyamoya disease (MMD) with different disease types and different bypass. **Methods** A total of 44 patients with MMD treated in Beijing Tiantan Hospital Affiliated to Capital Medical University from January 2010 to October 2011 were enrolled. All patients underwent cerebral revascularization. The improvement of neurological function was evaluated by National Institutes of Health Stroke Scale (NIHSS) 3 months after surgery, and the improvement of clinical symptoms was observed. DSA or CTA were reviewed to determine whether the bridge vessels were unobstructed and surgical complications were recorded. **Results** DSA or CTA reexamination showed that the anastomosis was unobstructed, and no surgical complications occurred. Patients with MMD were divided into 3 groups according to the onset type: ischemic, hemorrhagic and mixed. Compared with hemorrhagic type and mixed type, neurological function improved 3 months after surgery in patients with ischemic type ($\chi^2 = 3.853, P = 0.001$; $\chi^2 = 4.110, P = 0.001$) and improvement of clinical symptoms ($\chi^2 = 3.934, P = 0.000$; $\chi^2 = 4.138, P = 0.000$) were better. According to the operation type, the patients were divided into 4 groups: anterior-frontal, anterior-temporal, posterior-frontal and posterior-temporal bypass. The improvement of neurological function in anterior-frontal bypass group was higher than that in anterior-temporal bypass group ($\chi^2 = 2.079, P = 0.038$). The improvement of neurological function and clinical symptoms in posterior-frontal bypass group were higher than those in anterior-temporal bypass group ($\chi^2 = 2.909, P = 0.004$; $\chi^2 = 2.812, P = 0.005$), and those in posterior-frontal bypass group were also higher than those in posterior-temporal bypass group

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($\chi^2 = 2.295, P = 0.022; \chi^2 = 2.580, P = 0.010$). **Conclusions** Compared with the other 2 groups, symptoms of ischemic MMD may improved better than before, and the intraoperative selection of posterior-frontal and anterior-frontal bypass may be better than anterior-temporal and posterior-temporal bypass.

【Key words】 Moyamoya disease; Cerebral revascularization; Temporal arteries; Middle cerebral artery; Prognosis

Conflicts of interest: none declared

烟雾病(MMD)系一种独特的脑血管病,其特征是进行性颅内动脉狭窄和小血管侧支代偿,后者在脑血管造影上形成特征性烟雾状外观,故而得名^[1]。烟雾病致急性缺血性卒中的急性期治疗主要是对症治疗,旨在降低颅内压、改善脑血流量(CBF)和控制癫痫发作等^[2]。目前尚无特发性烟雾病的治疗方法,针对症状性烟雾病的二级预防主要采用脑血管重建术^[3]。大多数情况下,烟雾病呈进展性,并不因服用抗血小板药或血管扩张药而缓解,外科手术可以通过改善脑循环降低缺血性或出血性卒中的风险^[4],分为直接搭桥术、间接搭桥术和直接联合间接搭桥术^[5]。直接搭桥术主要包括颞浅动脉-大脑中动脉(STA-MCA)搭桥术,桥血管血流通畅率高达94%~100%,是成人烟雾病致缺血性卒中的推荐术式^[6-7];间接搭桥术主要包括颅骨多点钻孔术(MBH)、脑-颞肌贴敷术(EMS)、脑-动脉贴敷术(EDS)、脑-硬膜-动脉-颞肌贴敷术(EDAMS)等^[8],特别在与受体动脉无法吻合的情况下,可随时间的推移促进新生血管发展^[9]。尽管STA-MCA搭桥术联合脑-动脉贴敷术在颅内动脉闭塞性疾病中的有效性已经证实^[10],但术式的选择取决于术者手术专长、经验以及术中解剖、技术限制等,始终存在一定争议。基于此,本研究回顾分析首都医科大学附属北京天坛医院近2年连续收治的44例烟雾病患者临床资料,对比分析不同发病类型和不同术式的短期预后,以期对临床选择烟雾病脑血管重建术式有所提示。

对象与方法

一、研究对象

1. 纳入与排除标准 (1)烟雾病的诊断符合2012年日本烟雾病(Willis环自发性闭塞)诊断与治疗指南^[1],并经DSA或MRI证实。(2)采用直接搭桥术或直接联合间接搭桥术。(3)排除保守治疗或仅行间接搭桥术、因颅内出血先行血肿清除术、临床资料不完整和失访患者。

2. 一般资料 选择2010年1月至2011年10月在我院神经外科住院治疗的烟雾病患者共44例,男性21例,女性23例;年龄为18~60岁,平均为(30.84±13.83)岁;病程1~240个月,中位病程为7(3,24)个月。

二、治疗方法

1. 术前评估 记录患者发病类型,DSA判断病变侧别并进行Suzuki分期,1期,颈内动脉狭窄期,仅颈内动脉分叉部狭窄;2期,“烟雾”状血管初发期,脑底出现“烟雾”状血管,伴所有主要动脉扩张;3期,“烟雾”状血管发展加重期,大脑前动脉和大脑中动脉血流量减少;4期,“烟雾”状血管形状缩小期,大脑后动脉近端受累;5期,“烟雾”状血管减少期,所有主要动脉消失;6期,“烟雾”状血管消失期,脑循环完全由颈外动脉系统提供。

2. STA-MCA搭桥术联合脑-动脉贴敷术 患者仰卧位,气管插管全身麻醉,头部偏向对侧、同侧肩部垫软垫。在MRI和CT灌注成像(CTP)显示的缺血较重区域沿颞浅动脉走行做“Y”形或弧形切口,皮下完全游离颞浅动脉前支和后支并保持通畅;沿颞浅动脉主干“T”形切开颞肌并向两侧牵拉,充分显露颅骨并制备骨窗;切开硬脑膜,保留脑膜中动脉,以侧裂上下颞上回和额下回大脑中动脉M4段为受体动脉,优先选择直径较大(0.80~1.50 mm)、管壁质地较好的节段,根据颞浅动脉前支和后支直径、走行和长度,以与受体动脉相匹配的分支为供血动脉,临时动脉瘤夹阻断受体动脉,竖行切开动脉表面,将颞浅动脉与M4段端侧吻合,间断缝合或连续缝合,术中吻合血管后即行吲哚菁绿荧光血管造影术(ICGA)以确认桥血管血流通畅;将硬脑膜翻转贴敷于脑表面,骨瓣复位固定,确保颞浅动脉未受压闭塞,逐层缝合颞肌、皮下及头皮。

3. 预后评估 (1)神经功能:分别于出院时和术后3个月行美国国立卫生研究院卒中量表(NIHSS)评分,以二者差值(术后3个月NIHSS评分-出院时NIHSS评分)评估神经功能改善情况,差值>0,神经

功能障碍加重;差值为零,无变化;差值 < 0,神经功能改善;且差值绝对值越大、神经功能变化越显著。(2)临床症状:电话随访至术后 3 个月,据患者主观描述分为,临床症状完全消失或未再发生短暂性脑缺血发作(TIA)、临床症状好转但未消失、临床症状无变化、临床症状加重或出现新症状,其中前两项定义为临床症状改善。(3)桥血管通畅率:术后 3 个月复查 DSA 或 CTA,评估桥血管通畅率。(4)安全性:记录术中和术后 3 个月手术相关并发症发生率,包括围手术期脑卒中、脑过度灌注综合征(CHS)等。

4. 统计分析方法 采用 SPSS 19.0 统计软件进行数据处理与分析。术后 3 个月 NIHSS 评分改变和临床症状为有序等级资料,以率(%)表示,采用 Mann-Whitney *U* 检验或 Kruskal-Wallis 检验(*H* 检验),两两比较行 Mann-Whitney *U* 检验。以 $P \leq 0.05$ 为差异具有统计学意义。

结 果

本组 44 例患者,以缺血性卒中发病 32 例(72.73%),以出血性卒中发病 7 例(15.91%),以缺血性和出血性卒中混合发病 5 例(11.36%);病变位于左侧 1 例(2.27%),右侧 2 例(4.55%),双侧 41 例(93.18%);术前 Suzuki 分期 1 期为 2 例(4.55%),2 期 7 例(15.91%),3 期 19 例(43.18%),4 期 9 例(20.45%),5 期 6 例(13.64%),6 期 1 例(2.27%)。采取 STA-MCA 搭桥术 32 例(72.73%)以及 STA-MCA 搭桥术联合脑-动脉贴敷术 12 例(27.27%);术式分别为颞浅动脉前支-额侧大脑中动脉 M4 段(前-额)搭桥术 13 例(29.55%),颞浅动脉前支-颞侧大脑中动脉 M4 段(前-颞)搭桥术 7 例(15.91%),颞浅动脉后支-额侧大脑中动脉 M4 段(后-额)搭桥术 16 例(36.36%)以及颞浅动脉后支-颞侧大脑中动脉 M4 段(后-颞)搭桥术 8 例(18.18%)。术后 3 个月随访时,22 例(50%)神经功能改善(NIHSS 评分差值 < 0);临床症状消失或未再发生短暂性脑缺血发作 24 例(54.55%),临床症状好转但未消失 17 例(38.64%),临床症状无变化 2 例(4.55%),临床症状加重或出现新症状 1 例(2.27%);DSA 或 CTA 显示桥血管始终保持通畅;无一例发生手术相关并发症。

根据发病类型将患者分为缺血型、出血型和混合型 3 组,各组患者神经功能($P = 0.000$)和临床症状($P = 0.000$)改善情况差异具有统计学意义(表 1),

表 1 不同发病类型组患者术后 3 个月神经功能和临床症状改善情况的比较

Table 1. Comparison of neurological function and clinical symptoms improvement at 3 months after surgery in MMD patients with different disease types

组别	例数	NIHSS 评分改善	临床症状改善
缺血型[例(%)]	32	15(46.88)	30(93.75)
出血型(例)	7	3/7	6/7
混合型(例)	5	4/5	5/5
χ^2 值		27.474	28.213
<i>P</i> 值		0.000	0.000

NIHSS, National Institutes of Health Stroke Scale, 美国国立卫生研究院卒中量表。The same for tables below

表 2 不同发病类型组患者术后 3 个月神经功能和临床症状改善情况的两两比较

Table 2. Pairwise comparison of neurological function and clinical symptoms improvement at 3 months after surgery in MMD patients with different disease types

组间两两比	NIHSS 评分改善		临床症状改善	
	<i>Z</i> 值	<i>P</i> 值	<i>Z</i> 值	<i>P</i> 值
缺血型:出血型	3.853	0.000	3.934	0.000
缺血型:混合型	4.110	0.000	4.138	0.000
出血型:混合型	0.236	0.814	0.594	0.552

其中,缺血型患者神经功能($P = 0.000, 0.000$)和临床症状($P = 0.000, 0.000$)改善优于出血型和混合型患者(表 2)。

据术式分为前-额搭桥术、前-颞搭桥术、后-额搭桥术和后-颞搭桥术 4 组,各组患者神经功能($P = 0.012$)和临床症状($P = 0.011$)改善情况差异具有统计学意义(表 3),其中,前-额搭桥术组患者神经功能改善情况优于前-颞搭桥术组($P = 0.038$),后-额搭桥术组患者神经功能和临床症状改善情况分别优于前-颞搭桥术组($P = 0.004, 0.005$)和后-颞搭桥术组($P = 0.022, 0.010$;表 4)。

讨 论

烟雾病可以缺血性卒中、出血性卒中以及缺血性和出血性卒中混合发病,其脑血管搭桥术式的选择仍存争议,不同发病类型和不同术式的预后亦未明确。本研究对比分析不同发病类型和不同术式的烟雾病患者脑血管搭桥术后短期预后,结果显示,缺血型患者术后 3 个月神经功能和临床症状改善情况优于出血型和混合型患者,行后-额搭桥术的患者术后 3 个月神经功能和临床症状改善情况优于

表 3 不同术式组患者术后 3 个月神经功能和临床症状改善情况的比较(例)

Table 3. Comparison of neurological function and clinical symptoms improvement at 3 months after surgery in MMD patients with different bypass types (case)

组别	例数	NIHSS 评分改善	临床症状改善
前-额搭桥术(1)	13	8/13	13/13
前-颞搭桥术(2)	7	3/ 7	7/ 7
后-额搭桥术(3)	16	8/16	15/16
后-颞搭桥术(4)	8	3/ 8	6/ 8
χ ² 值		10.955	11.232
P 值		0.012	0.011

表 4 不同术式组患者术后 3 个月神经功能和临床症状改善情况的两两比较

Table 4. Pairwise comparison of neurological function and clinical symptoms improvement at 3 months after surgery in MMD patients with different bypass types

组间两两比	NIHSS 评分改善		临床症状改善	
	Z 值	P 值	Z 值	P 值
(1) : (2)	2.079	0.038	1.779	0.075
(1) : (3)	0.920	0.357	1.179	0.238
(1) : (4)	1.447	0.148	1.506	0.132
(2) : (3)	2.909	0.004	2.812	0.005
(2) : (4)	0.627	0.530	0.304	0.761
(3) : (4)	2.295	0.022	2.580	0.010

前-颞搭桥术和后-颞搭桥术,行前-额搭桥术的患者术后 3 个月神经功能改善亦优于前-颞搭桥术。

脑血管搭桥术的术式选择主要与术者经验和术中解剖所见相关,应采取个体化原则,不能一概而论^[2-3]。对于儿童烟雾病患者,颅骨多点钻孔术、脑-硬膜-动脉-颞肌贴敷术等间接搭桥术可在术后建立颞深动脉、颞浅动脉和脑膜中动脉侧支代偿,从而改善预后^[4];针对成人烟雾病患者,Meta 分析显示,与间接搭桥术相比,16 岁以上患者采取直接搭桥术或直接联合间接搭桥术可更为有效地预防脑卒中的发生,降低脑卒中的风险^[5];亦有学者提出,不管是儿童还是成年患者均宜行直接联合间接搭桥术,可以更好地改善脑灌注,长期预后更佳^[6-9]。本研究患者脑血管搭桥术均于 2010-2011 年完成,该时期主要采取单纯直接搭桥术(72.73%, 32/44),仅 27.27%(12/44)患者采取直接搭桥术联合一种间接搭桥术;近年来,首都医科大学附属北京天坛医院的闭塞性脑血管病主要采取直接搭桥术联合一种或多种间接搭桥术,包括颅骨多点钻孔术、脑-颞

肌贴敷术、脑-硬膜-动脉贴敷术等,以增加侧支循环,提高侧支代偿能力。但是由于难以针对术式开展大规模的随机对照临床试验,多数证据来自回顾性病例系列研究和病例报告。目前正在进行的日本无症状烟雾病登记(AMORE)研究有望获得更多的证据^[10-11]。

烟雾病脑血管搭桥术的预后受多种因素影响。研究显示,术前 Suzuki 分期($OR = 1.669, 95\%CI: 1.059 \sim 2.632; P = 0.027$)、以缺血性卒中发病($OR = 5.845, 95\%CI: 1.654 \sim 20.653; P = 0.006$)是术后发生脑缺血的危险因素^[12-13];入院时改良 Rankin 量表(mRS)评分、术前脑缺血症状与烟雾病患者术后脑过度灌注综合征相关^[14]。Zhao 等^[13]的研究显示,与术前 Suzuki 分期 1~2 期患者相比,Suzuki 分期 3~4 期患者术后短期症状加重、新发脑梗死风险增加,但长期随访发现,不管术前 Suzuki 分期处于何期,行直接搭桥术的患者长期预后趋势相近,临床症状改善、mRS 评分降低。研究显示,术前脑卒中、术中颞浅动脉外膜剥脱程度、围手术期血压降低、患者自身运动功能代偿可塑性等均与烟雾病脑血管搭桥术后远期预后相关^[15-18]。本研究对比分析不同发病类型以及不同术式的烟雾病患者脑血管搭桥术后短期预后,结果显示,术后 3 个月缺血型患者神经功能和临床症状改善情况优于出血型和混合型患者,究其原因,可能与本研究纳入对象术前 Suzuki 分期相对较早、脑缺血症状相对较轻有关;术后 3 个月行后-额搭桥术的患者神经功能和临床症状改善情况均优于前-颞搭桥术和后-颞搭桥术,行前-额搭桥术的患者神经功能改善亦优于前-颞搭桥术,推测是由于烟雾病患者主要在侧裂相邻区域行脑血管搭桥术,后-额搭桥术和前-额搭桥术后桥血管在额叶的供血范围更大^[2];此外,本研究预后评估采用 NIHSS 量表评价神经功能改善情况,主要包括意识、肢体活动、语言功能等,提示额叶恢复血供可能与症状改善有关^[19-20]。

本研究样本量较少且缺乏术中脑血流动力学指标分析,但为同一术者手术且术式相对统一,手术差异导致预后差异的可能性较小,因此本研究结论对临床有一定的提示意义。

利益冲突 无

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· 小词典 ·

中英文对照名词词汇(一)

白细胞介素-6 interleukin-6(IL-6)
 白细胞介素-4受体 interleukin-4 receptor(IL-4R)
 半数抑制浓度 half-inhibitory concentration(IC₅₀)
 北美症状性颈动脉内膜切除术试验
 North American Symptomatic Carotid Endarterectomy Trial
 (NASCET)
 EB病毒 Epstein Barr virus(EBV)
 病原相关分子模式
 pathogen-associated molecular pattern(PAMP)
 不对称皮质静脉征 asymmetrical cortical vein sign(ACVS)
 不对称髓静脉征 asymmetrical medullary vein sign(AMVS)
 不对称显著的皮质静脉征
 asymmetrically prominent cortical veins(APCVs)

长程视频脑电图
 long-term video electroencephalogram(LT-VEEG)
 出血性转化 hemorrhagic transformation(HT)
 磁共振静脉血管造影术
 magnetic resonance venography(MRV)
 磁敏感加权成像 susceptibility-weighted imaging(SWI)
 磁敏感血管征 susceptibility vessel sign(SVS)
 大动脉粥样硬化 large artery atherosclerosis(LAA)
 大脑后动脉 posterior cerebral artery(PCA)
 大脑前动脉 anterior cerebral artery(ACA)
 大脑中动脉 middle cerebral artery(MCA)
 大脑中动脉闭塞 middle cerebral artery occlusion(MCAO)
 大隐静脉 great saphenous vein(GSV)