

· 急性缺血性卒中血管内治疗 ·

急性缺血性卒中血管内机械取栓单中心临床研究

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【摘要】目的 探讨血管内机械取栓治疗大血管闭塞致急性缺血性卒中的有效性和安全性。**方法** 共41例大血管闭塞致急性缺血性卒中患者采用血管内机械取栓治疗,记录发病至入院时间、入院至股动脉穿刺时间、发病至血管再通时间,术后即刻采用改良脑梗死溶栓血流分级(mTICI)评价血管再通情况,术后24 h采用美国国立卫生研究院卒中量表(NIHSS)评价神经功能,术后90 d采用改良Rankin量表(mRS)评价临床预后;记录围手术期血管内机械取栓相关并发症,术后90 d症状性颅内出血发生率和病死率;采用美国介入和治疗性神经放射学学会/美国介入放射学学会侧支循环分级系统评价前循环侧支代偿,BATMAN评分标准评价后循环侧支代偿。**结果** 41例患者中12例(29.27%)行静脉溶栓桥接血管内机械取栓。32例(78.05%)术后即刻实现血管再通(mTICI 2b~3级),前循环再通20例(80%,20/25)、后循环再通12例(12/16),组间差异无统计学意义(校正 $\chi^2=1.424, P=0.706$)。28例(68.29%)术后24 h神经功能改善(NIHSS评分下降≥4分),前循环闭塞18例(72%,18/25)、后循环闭塞10例(10/16),组间差异无统计学意义($\chi^2=0.407, P=0.524$)。11例(26.83%)术后90 d内死亡,前循环闭塞4例(16%,4/25)、后循环闭塞7例(7/16),组间差异无统计学意义(校正 $\chi^2=2.130, P=0.144$)。3例死于并发肺部感染和呼吸功能衰竭、8例死于缺血性卒中;14例(34.15%)预后良好(mRS评分≤2分),前循环闭塞10例(47.62%,10/21)、后循环闭塞4例(4/9),组间差异无统计学意义(校正 $\chi^2=0.493, P=0.483$)。6例(14.63%)发生症状性颅内出血,前循环闭塞4例(16%,4/25)、后循环闭塞2例(2/16),组间差异无统计学意义(校正 $\chi^2=3.303, P=0.856$)。33例行侧支代偿评价,20例前循环闭塞患者中14例(70%)侧支代偿良好,其中9例(9/14)术后90 d预后良好,6例(30%)侧支代偿欠佳均预后不良,组间差异有统计学意义(Fisher确切概率法: $P=0.014$)。13例后循环闭塞患者中3例(3/13)侧支代偿良好,术后90 d均预后良好,10例(10/13)侧支代偿欠佳,仅1例(1/10)预后良好,组间差异有统计学意义(Fisher确切概率法: $P=0.014$)。**结论** 血管内机械取栓用于治疗大血管闭塞致急性缺血性卒中安全、有效,严格把握手术适应证、充分进行术前评估、完善脑卒中救治流程可以提高血管内机械取栓疗效。

【关键词】 卒中; 脑缺血; 血栓切除术; 血管造影术,数字减影

A single-center study on endovascular thrombectomy for acute ischemic stroke

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【Abstract】 Objective To evaluate the efficiency and safety of endovascular thrombectomy for acute ischemic stroke caused by acute large vessel occlusion. **Methods** A total of 41 patients with acute ischemic stroke caused by acute large vessel occlusion were treated with endovascular thrombectomy. Time from onset to admission, from admission to femoral artery puncture, from onset to recanalization were recorded. Modified Thrombolysis in Cerebral Infarction (mTICI) was used to assess the recanalization immediately after operation. National Institutes of Health Stroke Scale (NIHSS) was used to evaluate the neurological function at 24 h after operation. Modified Rankin Scale (mRS) was used to evaluate clinical prognosis at 90 d after operation. Perioperative procedure-related complications and occurrence rate of symptomatic intracranial hemorrhage within at 90 d after operation were recorded. American Society of

doi:10.3969/j.issn.1672-6731.2017.11.005

基金项目:吴阶平医学基金会临床科研专项课题(项目编号:320.6750.12189)

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Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) Collateral Flow Grading System (ACG) was used to assess collateral compensation of anterior circulation. BATMAN score was used to assess collateral compensation of posterior circulation. **Results** Among 41 patients, 12 (29.27%) were treated with recombinant tissue-type plasminogen activator (rt-PA) intravenous thrombolysis. There were 32 patients (78.05%) achieved successful recanalization, including 20 patients (80%, 20/25) in anterior circulation and 12 (12/16) in posterior circulation, and no significant difference was seen between them (adjusted $\chi^2 = 1.424$, $P = 0.706$). At 24 h after operation, 28 patients (68.29%) had better neurological function than preoperation (NIHSS decreasing ≥ 4 score), including 18 patients (72%, 18/25) with anterior circulation occlusion and 10 (10/16) with posterior circulation occlusion, and there was no significant difference between them ($\chi^2 = 0.407$, $P = 0.524$). Eleven patients (26.83%) died within 90 d after operation, including 4 patients (16%, 4/25) with anterior circulation occlusion and 7 (7/16) with posterior circulation occlusion, and there was no significant difference between them (adjusted $\chi^2 = 2.130$, $P = 0.144$). Among the 11 dead, 3 died of complicated pulmonary infection and respiratory failure, and 8 died of ischemic stroke. The other 30 patients were followed up for 3 months to one year, average (231.92 ± 95.36) d. At 90 d after operation, 14 patients (34.15%) had good outcome (mRS ≤ 2 score), including 10 patients (47.62%, 10/21) with anterior circulation occlusion and 4 (4/9) with posterior circulation occlusion, and there was no significant difference between them (adjusted $\chi^2 = 0.493$, $P = 0.483$). Among 41 patients, 6 patients (14.63%) had symptomatic intracranial hemorrhage, including 4 patients (16%, 4/25) with anterior circulation occlusion and 2 (2/16) with posterior circulation occlusion, and no significant difference was seen between them (adjusted $\chi^2 = 3.303$, $P = 0.856$). Collateral compensation was evaluated in 33 patients (20 with anterior circulation occlusion and 13 with posterior circulation occlusion). In 20 patients with anterior circulation occlusion, 14 patients (70%) had good collateral compensation, in whom 9 (9/14) had good outcome 90 d after operation, while the other 6 patients (30%) had poor collateral compensation and then had good outcome 90 d after operation, and significant difference was seen between them (Fisher exact probability: $P = 0.014$). Among 13 patients with posterior circulation occlusion, 3 patients (3/13) had good collateral compensation and had good outcome 90 d after operation, while the other 10 (10/13) had poor collateral compensation, in whom one (1/10) had good outcome 90 d after operation, and significant difference was seen between them (Fisher exact probability: $P = 0.014$). **Conclusions** Endovascular thrombectomy is an efficient and safe method for acute ischemic stroke caused by acute large vessel occlusion. Rigorously master the indication and preoperative evaluation, and perfect acute rescue procedure and treatment for stroke may increase the efficacy of endovascular thrombectomy.

【Key words】 Stroke; Brain ischemia; Thrombectomy; Angiography, digital subtraction

This study was supported by Wu Jieping Medical Foundation Clinical Research Special Project (No. 320.6750.12189).

近几十年来,脑卒中已经跃升为全球第3位、我国首位致死性疾病,并具有极高的病残率,严重威胁我国居民健康,给患者家庭和社会带来沉重负担。2017年公布的我国脑卒中流行病学调查研究显示,脑卒中年龄标化发病率为246.8/10万、年龄标化病死率为114.8/10万,我国东北地区脑卒中形势更加严峻,发病率高达365.2/10万,脑卒中预防与治疗刻不容缓^[1]。研究显示,60%~80%的脑卒中为缺血性卒中,传统治疗方法为静脉溶栓,但大血管闭塞导致的急性缺血性卒中静脉溶栓效果欠佳^[2]。自2015年以来,血管内机械取栓作为大血管闭塞致急性缺血性卒中的首选治疗方法,经多项大规模前瞻性随机对照临床试验证实,并被多个国家的脑卒中治疗指南以高级别证据强烈推荐^[3-4]。本研究回顾分析近年来在哈尔滨医科大学附属第一医院神

经外科采用血管内机械取栓治疗的大血管闭塞致急性缺血性卒中患者的临床资料,探讨血管内机械取栓的有效性和安全性,以为临床开展该项技术提供依据。

资料与方法

一、临床资料

1. 纳入标准 (1)急性缺血性卒中的诊断符合《中国急性缺血性脑卒中诊治指南2014》^[5]。(2)经头部CT排除颅内出血。(3)经MRA或数字减影血管造影术(DSA)证实颈内动脉(ICA)、椎-基底动脉或大脑中动脉(MCA)M1段闭塞。(4)入院时美国国立卫生研究院卒中量表(NIHSS)评分>6分。(5)发病前改良Rankin量表(mRS)评分<2分。(6)本研究经哈尔滨医科大学附属第一医院道德伦理委员会审

核批准,所有患者或其家属均知情同意并签署知情同意书。

2. 排除标准 存在血管内治疗禁忌证的患者;合并重要脏器功能衰竭的患者。

3. 一般资料 选择2015年1月~2017年6月在哈尔滨医科大学附属第一医院神经外科采用血管内机械取栓治疗的大血管闭塞致急性缺血性卒中患者共41例,男性33例,女性8例;年龄37~85岁,平均(59.51 ± 12.88)岁;既往有高血压21例(51.22%)、糖尿病8例(19.51%)、心房颤动10例(24.39%)、高脂血症3例(7.32%),吸烟14例(34.15%);均经DSA证实为急性大血管闭塞,其中大脑中动脉闭塞15例(36.59%)、颈内动脉闭塞6例(14.63%)、颈内动脉起始部和同侧大脑中动脉串联闭塞4例(9.76%)、基底动脉闭塞12例(29.27%)、优势侧椎动脉和基底动脉串联闭塞4例(9.76%),前循环闭塞25例(60.98%)、后循环闭塞16例(39.02%);11例(26.83%)存在原发性颅内动脉重度狭窄,其中前循环闭塞5例、后循环闭塞6例;入院时NIHSS评分5~38分,中位评分20(14,28)分;发病前mRS评分0~1分,中位评分0(0,0)分;Alberta脑卒中计划早期CT评分(ASPECTS)0~10分,中位评分8(6,10)分。

二、研究方法

1. 血管内机械取栓 患者仰卧位,于气管插管全身麻醉或质量分数为2%利多卡因5 ml局部麻醉下,经股动脉穿刺,置入8F动脉鞘(日本Terumo公司),8F Mach1导引导管(美国Boston Scientific公司)置于患侧颈内动脉岩段(前循环闭塞患者)或患侧锁骨下动脉(后循环闭塞患者),再将5F Navien导管(美国EV3公司)置于病变近端;以0.014英寸Tracess微导丝(美国MicroVention公司)配合Rebar18微导管(美国EV3公司)通过闭塞段血管,撤出微导丝后行超选择性DSA证实微导管位于病变远端血管腔后,经微导管释放Solitaire AB支架(美国EV3公司),静置5 min后负压抽吸,回撤支架,即刻行DSA检查,直至闭塞血管远端血流恢复至改良脑梗死溶栓血流分级(mTICI)≥2b级方结束手术。对于存在动脉粥样硬化性狭窄的患者,取栓后观察15~20 min,如果血管再通较取栓后即刻无明显变化则结束手术;如果难以维持mTICI分级≥2b级,则采用球囊扩张术和(或)支架植入术。球囊扩张采用Gateway球囊(美国Boston

Scientific公司)置于狭窄处,扩张后即刻行DSA检查,直至血流达mTICI分级≥2b级,观察15 min血流无变化后结束手术;若球囊扩张后血流仍难以达mTICI分级≥2b级,则植入Apollo球囊扩张式支架(中国微创医疗公司)后结束手术。

2. 静脉溶栓治疗 对于符合《中国急性缺血性脑卒中诊治指南2014》^[5]中静脉溶栓适应证、无禁忌证的患者及时予以重组组织型纤溶酶原激活物(rt-PA)0.90 mg/kg静脉溶栓治疗。

3. 药物治疗 术后常规予双联抗血小板治疗(阿司匹林100 mg/d和氯吡格雷75 mg/d),连续3个月后改为阿司匹林100 mg/d长期服用。对于存在原发性颅内动脉重度狭窄的患者,术后予替罗非班0.10 μg/(kg·min)持续静脉滴注24 h后,再予常规抗血小板治疗。

4. 有效性和安全性评价 (1)有效性评价:记录发病至入院时间、入院至股动脉穿刺时间、发病至血管再通时间;术后即刻采用mTICI分级评价血管再通情况,2b~3级为血管再通;术后24 h采用NIHSS量表评价神经功能,NIHSS评分下降≥4分为神经功能改善;术后90 d采用mRS量表评价临床预后,≤2分为预后良好,>2分为预后不良。(2)安全性评价:记录围手术期血管内机械取栓相关并发症,包括非病变血管区域新发栓塞和股动脉假性动脉瘤等;术后90 d颅内出血发生率和病死率。症状性颅内出血定义为任意性质的颅内出血且NIHSS评分增加≥4分^[6]。

5. 影像学评价 术前采用ASPECTS评分评价核心梗死大小,术后即刻复查Xper CT,术后24 h复查CT。前循环侧支偿评价采用美国介入和治疗性神经放射学学会/美国介入放射学学会侧支循环分级系统(ASITN/SIR ACG)^[7-8],2~4级为侧支偿良好、0~1级为侧支偿欠佳;后循环侧支偿评价采用BATMAN评分标准^[9],7~10分为侧支偿良好、<7分为侧支偿欠佳。

三、统计分析方法

采用SPSS 19.0统计软件进行数据处理与分析。呈正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,呈非正态分布的计量资料以中位数和四分位数间距 [$M(P_{25}, P_{75})$] 表示;计数资料以相对数构成比(%)或率(%)表示,采用 χ^2 检验、校正 χ^2 检验或Fisher确切概率法。以 $P \leq 0.05$ 为差异具有统计学意义。

结 果

本组41例行血管内机械取栓患者中12例(29.27%)先予rt-PA静脉溶栓治疗。其中,25例前循环闭塞患者发病至入院时间0~360 min、中位时间135(70,237) min,入院至股动脉穿刺时间30~250 min、中位时间87(77,130) min,发病至血管再通时间163~570 min、中位时间311.00(242.50,416.00) min;16例后循环闭塞患者发病至入院时间30~720 min、中位时间135(104,285) min,入院至股动脉穿刺时间30~290 min、中位时间109(55,200) min,发病至血管再通时间230~975 min、中位时间360(281,460) min。32例(78.05%)术后即刻实现血管再通(mTICI分级2b~3级),其中前循环再通20例(80%,20/25)、后循环再通12例(12/16),组间差异未见统计学意义(校正 $\chi^2=1.424, P=0.706$);9例(21.95%)未实现血管开通,包括单纯基底动脉顶部闭塞3例、椎动脉和基底动脉串联闭塞1例、颈内动脉起始部和大脑中动脉串联闭塞3例、大脑中动脉M1段血栓破裂致远端栓塞2例。28例(68.29%)术后24 h神经功能改善(NIHSS评分下降≥4分),其中前循环闭塞18例(72%,18/25)、后循环闭塞10例(10/16),组间差异未见统计学意义($\chi^2=0.407, P=0.524$)。11例(26.83%)术后90 d内死亡,其中前循环闭塞4例(16%,4/25)、后循环闭塞7例(7/16),组间差异无统计学意义(校正 $\chi^2=2.130, P=0.144$),3例死因为并发肺部感染和呼吸功能衰竭、8例死因为缺血性卒中;其余30例随访3个月至1年、平均(231.92±95.36) d,术后90 d 14例(34.15%)临床预后良好(mRS评分≤2分),恢复生活自理能力,其中前循环闭塞10例(47.62%,10/21)、后循环闭塞4例(4/9),组间差异无统计学意义(校正 $\chi^2=0.493, P=0.483$)。41例患者中症状性颅内出血6例(14.63%),其中前循环闭塞4例(16%,4/25)、后循环闭塞2例(2/16),组间差异无统计学意义(校正 $\chi^2=3.303, P=0.856$);非病变血管区域新发栓塞1例(2.44%),为大脑中动脉闭塞患者。

本组41例患者中5例前循环闭塞和3例后循环闭塞患者缺乏侧支代偿影像学资料,对余33例患者的侧支代偿情况进行分析,结果显示,20例前循环闭塞患者中14例(70%)侧支代偿良好(ASITN/SIR ACG分级2~4级),其中9例(9/14)术后90 d临床预后良好,6例(30%)侧支代偿欠佳(ASITN/SIR ACG

分级0~1级)均临床预后不良,组间差异具有统计学意义(Fisher确切概率法: $P=0.014$);侧支代偿良好患者中1例(1/14)发生症状性颅内出血;侧支代偿欠佳患者中3例(3/6)发生症状性颅内出血,组间差异无统计学意义(Fisher确切概率法: $P=0.061$)。13例后循环闭塞患者中3例(3/13)侧支代偿良好(BATMAN评分7~10分),术后90 d临床预后良好,10例(10/13)侧支代偿欠佳(BATMAN评分<7分),仅1例(1/10)临床预后良好,组间差异具有统计学意义(Fisher确切概率法: $P=0.014$)。侧支代偿良好患者未发生症状性颅内出血;侧支代偿欠佳患者中2例(2/10)发生症状性颅内出血,组间差异无统计学意义(Fisher确切概率法: $P=0.100$)。

讨 论

2015年,*N Engl J Med*发表5项血管内治疗大血管闭塞致急性缺血性卒中的随机对照临床试验,包括血管内治疗缺血性卒中的多中心随机临床试验(MR CLEAN)^[10]、延长急性神经功能缺损至动脉内溶栓时间的临床试验(EXTEND-IA)^[11],前循环近端闭塞小病灶性卒中的血管内治疗并强调最短化CT扫描至再通时间临床试验(ESCAPE)^[12],血管内机械取栓作为急性缺血性卒中血管内主要治疗试验(SWIFT PRIME)^[13],西班牙8小时内支架取栓与内科治疗随机对照试验(REVASCAT)^[14],使血管内机械取栓成为缺血性卒中治疗领域最受关注的治疗方法,但各项研究报道的治疗果存在一定差距。MR CLEAN试验是首个证实血管内机械取栓治疗前循环大血管闭塞致急性缺血性卒中有效的临床研究,约32.62%(76/233)患者术后90天恢复生活自理能力^[10],经过更严格的术前评估、限定核心梗死大小和缺血半暗带区大小、排除侧支代偿欠佳患者后,血管内机械取栓疗效提高至43.70%(52/119)~71.43%(25/35)^[11-12,14]。然而,上述研究为多中心临床试验,不能准确反映出不同地区、不同医疗中心的血管内机械取栓疗效;且主要针对前循环大血管闭塞,血管内机械取栓治疗椎-基底动脉闭塞致急性缺血性卒中的疗效尚未明确。

本研究41例行血管内机械取栓治疗的大血管闭塞致急性缺血性卒中患者中32例(78.05%)术后即刻血管再通,28例(68.29%)术后24小时神经功能改善,14例(34.15%)术后90天恢复生活自理能力,证实血管内机械取栓治疗大血管闭塞致急性缺

血性卒中的有效性。有文献报道,术前 ASPECTS 评分与预后明显相关^[15]。本研究 41 例患者中 28 例(68.29%)术前 ASPECTS 评分 ≥ 6 分,其中 12 例(42.86%)临床预后良好。分组分析显示,前循环闭塞组有 10 例(40%, 10/25)血管内机械取栓后 90 天恢复生活自理能力,后循环闭塞组仅 4 例(4/16),但是并不意味着血管内机械取栓对急性椎-基底动脉闭塞的疗效欠佳,这是由于椎-基底动脉闭塞患者病残率和病死率高达 70%^[16],本研究后循环闭塞组有 10 例(10/16)术后 24 小时神经功能改善,提示血管内机械取栓对椎-基底动脉闭塞致急性缺血性卒中同样安全、有效。

既往研究显示,具有良好侧支代偿的患者更容易获得良好预后^[17]。目前评价前循环侧支代偿的主要方法包括 CTA、CT 灌注成像(CTP)、多模式 CT 等,对侧支代偿的评价有利于预测前循环大血管闭塞致急性缺血性卒中患者的预后和症状性颅内出血发生率,但目前尚无统一评价方法。本研究通过 DSA 检查,采用 ASITN/SIR ACG 分级评价前循环侧支代偿、BATMAN 评分标准评价后循环侧支代偿,结果显示,侧支代偿欠佳的患者术后 90 天临床预后不良、症状性颅内出血发生率高,为国内不具备随时行 CTA 检查条件的医疗中心提供参考依据,但是本研究样本量较小,尚待扩大样本量的研究证实。

本研究结果与 EXTEND-IA 试验和 ESCAPE 试验等的结果存在一定差距,65.85%(27/41)患者即使采用血管内机械取栓仍无法获得良好预后,如何能够提高血管内机械取栓的有效性仍是神经外科医师面临的棘手问题。本研究前循环闭塞患者发病至入院时间为 135(70,237)分钟、后循环闭塞患者为 135(104,285)分钟,远超过上述 5 项临床研究的 85~127 分钟;前循环闭塞患者入院至股动脉穿刺时间 87(77,130)分钟、后循环闭塞患者 109(55,200)分钟,略高于《急性缺血性卒中血管内治疗中国指南 2015》^[4]建议的 60~90 分钟,提示院内急救流程有待改善。因此,提高脑卒中治疗效果需要整个脑卒中救治流程的完善,从院前急救到院内脑卒中绿色通道,缩短检查和术前评估时间,进一步提高大血管闭塞致急性缺血性卒中的治疗效果^[18]。

综上所述,严格把握手术适应证、充分进行术前评估、完善脑卒中救治流程是提高血管内机械取栓治疗大血管闭塞致急性缺血性卒中疗效的可行措施。

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(收稿日期:2017-10-23)

·小词典·

中英文对照名词词汇(三)

美国卒中协会 American Stroke Association(ASA)

门-针时间 door to needle time(DNT)

脑白质高信号 white matter hyperintensity(WMH)

脑梗死溶栓血流分级

Thrombolysis in Cerebral Infarction(TICI)

脑血流量 cerebral blood flow(CBF)

Alberta 脑卒中计划早期 CT 评分

Alberta Stroke Program Early CT Score(ASPECTS)

脑卒中血管内治疗Ⅲ期临床

Interventional Management of Stroke III (IM3)

凝视-面-臂-语言-时间测验 Stare-Face-Arm-Speech-Time (S.F.A.S.T.)

Gaze-Face-Arm-Speech-TR

凝血酶原时间 prothrombin time(PT)

欧洲神经科学协会联盟

European Federation of Neurological Societies (EFNS)

帕金森病痴呆 Parkinson's disease dementia(PDD)

平均扩散率 mean diffusivity(MD)

平均树突长度 mean dendrite length(MDL)

其他明确病因 stroke of other determined etiology(SOE)

前循环近端闭塞小病灶性卒中的血管内治疗并强调

最短化CT扫描至再通时间临床试验

Endovascular Treatment for Small Core and Anterior Circulation Recanalization with Endovascular

Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times (ESCAPE) trial

腔隙性梗死 lacunar infarct(LACI)

轻度认知损害 mild cognitive impairment(MCI)

倾向性评分匹配法 propensity score matching(PSM)