

支架取栓与动脉溶栓治疗大脑中动脉栓塞超4.5小时患者的对比研究

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摘要 目的: 对比研究支架取栓与动脉溶栓治疗急性大脑中动脉栓塞超4.5 h患者的临床疗效。方法: 99例急性大脑中动脉栓塞超过4.5 h的患者按治疗方式分为溶栓组41例和取栓组58例。溶栓组接受选择性动脉溶栓治疗, 取栓组接受Solitaire支架进行机械取栓治疗, 手术结束前采用脑梗死溶栓试验(TICI)分级评价血管再通情况, 比较2组的手术时间; 采用美国国立卫生研究院卒中量表(NIHSS)评价2组患者的预后情况; 比较2组发生不良反应情况; 并于90 d进行随访。结果: 取栓组的血管再通率、完全再通率明显高于溶栓组(94.8% v.s. 78.0%, 67.2% v.s. 41.5%, 均 $P<0.05$); 取栓组的手术时间短于溶栓组($P<0.05$); 治疗后取栓组的NIHSS评分优于溶栓组($P<0.05$); 取栓组治疗后总有效率为96.6%, 高于溶栓组的87.8%($P<0.05$); 取栓组的基本治愈率高于溶栓组(50.0% v.s. 31.7%, $P<0.05$); 溶栓组患者的颅内出血的比例高于取栓组($P<0.05$); 90 d随访, 取栓组恢复优于溶栓组($P<0.05$)。结论: 支架取栓治疗可显著改善大脑中动脉栓塞超4.5 h患者的临床预后, 减少不良反应发生。

关键词 支架取栓; 动脉溶栓; 大脑中动脉; 栓塞

中图分类号 R741; R743.33 文献标识码 A DOI 10.16780/j.cnki.sjssgncj.2018.07.004

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收稿日期

2017-10-17

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Comparative Study of Stent Thrombectomy and Arterial Thrombolysis in Treatment of Patients with Middle Cerebral Artery Occlusion Over 4.5 Hours ZHOU Xiang-ling¹, PAN Chun-lian¹, CHENG Chao-hui²

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Abstract Objective: To compare the clinical efficacy of stent thrombectomy and arterial thrombolysis in the treatment of acute middle cerebral artery occlusion of more than 4.5 hours. **Methods:** Ninety-nine patients with acute middle cerebral artery occlusion were divided into the thrombolytic group (n=41) and the thrombectomy group (n=58) according to treatment method. Selective intra-arterial thrombolysis was performed on thrombolysis group patients, and mechanical thrombectomy using the Solitaire stent was performed on thrombectomy group patients. Thrombolysis in Cerebral Infarction (TICI) was used to evaluate the recanalization of vessels prior to the conclusion of surgery, and the operation time of the two groups was compared. The recovery of the two groups was evaluated by the National Institutes of Health Stroke Scale (NIHSS) score. Adverse reactions were recorded and followed up at 90 days. **Results:** The recanalization rate and complete recanalization rate of the thrombectomy group were significantly higher than those of thrombolysis group (94.8% v.s. 78.0, 67.2% v.s. 41.5%, both $P<0.05$). The operation time of the thrombectomy group was lower than that of the thrombolysis group ($P<0.05$). After treatment, the NIHSS score of the thrombectomy group was significantly better than that of the thrombolysis group ($P<0.05$). The total effective rate of the thrombectomy group was 96.6%, which was significantly higher than the 87.8% rate of the thrombolysis group ($P<0.05$). The cure rate of the thrombectomy group was significantly higher than that of the thrombolysis group (50.0% v.s. 31.7%, $P<0.05$). The patients in the thrombolysis group had a higher rate of intracranial hemorrhage than those in the thrombectomy group ($P<0.05$). At the 90-day follow-up, patients in the thrombectomy group showed better recovery than those in the thrombolysis group ($P<0.05$). **Conclusion:** Stent thrombectomy can significantly improve the clinical prognosis of patients with cerebral arterial embolization of over 4.5 hours.

Key words stenting thrombectomy; arterial thrombolysis; middle cerebral artery; embolization

脑梗死是脑部血液循环障碍引起的脑部功能异常, 常导致严重的后遗症^[1]。脑梗死一旦发生, 应尽快恢复缺血脑组织的血流, 挽救缺血半暗带的神经细胞, 发病4.5 h内给予rt-PA静脉溶栓治疗可取得良好的临

床疗效, 一旦堵塞时间超过4.5 h, 静脉溶栓不但不能救治濒临坏死的神经细胞, 反而容易引起脑出血加重病情^[2]。对于临床发病超过4.5 h的大脑中动脉闭塞目前主要采用选择性动脉溶栓和动脉内支架取栓治疗^[3]。与

静脉溶栓相比,血管内治疗时间窗更长,可直接作用于病灶部位,降低并发症,有利于预后^[4]。但目前关于选择性动脉溶栓治疗和支架机械取栓治疗大脑中动脉急性栓塞的直接对比研究较少。本研究收集并分析在我院采用上述两种治疗方法的患者的资料,比较两种治疗方式的治疗效果、安全性和预后情况。

1 资料与方法

1.1 一般资料

收集2014年1月至2015年12月期间在我院接受选择性动脉溶栓和支架机械取栓治疗的急性大脑中动脉闭塞患者99例,临床症状为突发意识不清、一侧肢体活动及感觉障碍、口角歪斜及言语不利等典型脑卒中表现。纳入标准:年龄40~70岁;首次发病,且发病时间4.5~8 h;影像学检查排除脑出血,且闭塞部位位于大脑中动脉主干;NIHSS评分 ≥ 8 分;血压可控制在180/110 mmHg(1 mmHg=0.133 kPa)水平以下;家属知情并签署同意书。排除标准:影像学检查显示脑出血或存在血管畸形等高出血风险;头颅CT显示大面积低密度病灶形成;意识障碍或生命体征不平稳;严重的心、肺、肝、肾功能障碍,难以耐受手术;患者长期应用抗凝药物,或对造影剂或溶栓药物过敏。全部患者随机分为溶栓组(接受选择性动脉溶栓治疗)和取栓组(接受支架机械取栓治疗)。①溶栓组41例,男25例,女16例;年龄46~69岁,平均(59.2 $\pm$ 9.7)岁;病程(4.0 $\pm$ 0.7) d;美国国立卫生研究院卒中量表(NIH stroke scale, NIHSS)评分(18.8 $\pm$ 8.1)分;糖尿病17例(41.5%),高血压21例(51.2%),高脂血症16例(39.0%);②取栓组58例,男32例,女26例;年龄44~68岁,平均(57.3 $\pm$ 10.3)岁;病程(5.1 $\pm$ 1.2) d;NIHSS评分(17.8 $\pm$ 9.6)分;糖尿病21例(36.2%),高血压29例(50.0%),高脂血症18例(31.0%)。2组资料比较差异无统计学意义($P>0.05$)。

1.2 方法

患者入院后,首先确定发病时间,完善相关辅助检查,控制血压、血糖,颅脑CT平扫排除脑出血,CTA初步明确大脑中动脉栓塞位置,快速准备进行动脉溶栓治疗或支架机械取栓治疗。选择性动脉溶栓治疗方法:患者术前全身肝素化处理(50 U/kg)。患者仰卧位,1%利多卡因局部浸润麻醉,Seldinger技术穿刺右侧股动脉,置入6F导管鞘,导丝引导下送入6F Guiding,迅速行全脑血管造影术,进一步明确血管堵塞位置,然后置入3F微导管,微导管末端尽可能地接近血栓,随后间断团注

rt-PA溶栓治疗,每次20~30 mg,间隔10 min复查DSA,明确血管是否恢复血流,血管再通后立即停止应用溶栓药物,若血管未通继续团注rt-PA,应用的最大剂量为90 mg,结束治疗后自然中和肝素。6 h后拔出动脉鞘,压迫止血,加压包扎。取栓组操作:穿刺方法如溶栓组,造影发现责任病灶,微导丝引导下将微导管穿过血栓到达闭塞血管的远端,造影明确血栓的长度,然后将Solitaire支架系统通过微导管送入血栓位置,支架系统释放5 min预计取到血栓后撤出支架并检查血栓,同时造影复查血管是否再通,可重复操作3次,然后撤出导管,余处理同溶栓组。2组术后常规服阿司匹林、氯吡格雷等双联抗血小板聚集治疗,并行抗血管痉挛、营养神经、扩容等治疗。

1.3 评价指标和随访

动脉溶栓和支架取栓后,采用脑梗死溶栓试验(Thrombolysis in Cerebral Infarction, TICI)分级评估脑血流灌注情况,TICI 0级、I级、II a为血管未再通,TICI II b~III级为血管再通^[5];记录患者从穿刺到血管再通的手术时间(puncture-to-reperfusion time, PRT);于治疗前及治疗后24 h、3 d、7 d进行NIHSS评分评估患者神经功能缺损情况,以7 d的NIHSS评分评价患者疗效^[6],以基本治愈、显效和有效计算总有效率。术后90 d进行门诊或电话随访,采用改良Rankin量表(modified Rankin scale, mRS)评估患者预后,mRS评分 ≤ 2 分为预后良好。患者术后第2天复查颅脑CT,明确是否存在颅内出血。治疗过程中,评估2组安全性,包括血栓脱落二次栓塞、颅内出血及症状性颅内出血发生率。

1.4 统计学处理

采用SPSS20.0统计学软件进行数据分析,计数资料采用 χ^2 检验;计量资料以($\bar{x}\pm s$)表示,2组治疗前后采用配对 t 检验,2组比较采用独立样本 t 检验, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 2组再通率及手术时间比较

血管内治疗结束前的造影显示,取栓组的血管再通率为94.8%(55/58),其中血管完全再通(TICI III级)39例,部分再通(TICI II b级)16例;溶栓组的血管再通率为78.0%(32/41),其中血管完全再通(TICI III级)17例,部分再通(TICI II b级)15例。取栓组的血管再通率、完全再通率高于溶栓组,差异有统计学意义($P<0.05$);取栓组的PRT时间短于溶栓组,差异有统计学意义($P<0.05$),见表1。

表1 2组再通率比较

组别	例数	TICI Ⅲ级/[例(%)]	TICI Ⅱb级/[例(%)]	TICI Ⅱa级/[例(%)]	TICI I /0级/[例(%)]	PRT/(min, $\bar{x}\pm s$)
溶栓组	41	17(41.5)	15(36.6)	4(9.76)	5(12.2)	81.90±40.91
取栓组	58	39(67.2) ^①	16(27.6)	2(3.45)	1(1.72) ^①	66.34±33.21 ^①

注:与溶栓组比较,^① $P<0.05$

2.2 2组NIHSS评分比较

2组治疗前的NIHSS评分差异无统计学意义($P>0.05$);治疗24 h、3 d、7 d,取栓组的NIHSS评分优于溶栓组,差异均有统计学意义($P<0.05$),见表2。2组经治疗7 d后取栓组的总有效率为96.6%,高于溶栓组的87.8%,差异有统计学意义($P<0.05$);基本治愈率(50.0%)也高于溶栓组(31.7%),差异有统计学意义($P<0.05$);无效率低于溶栓组,差异有统计学意义($P<0.05$),见表3。

2.3 随访情况比较

取栓组90 d良好预后比例高于溶栓组,差异有统计学意义(78.60%v.s.45.78%, $P<0.05$)。

2.4 安全性比较

取栓组的颅内出血比例和症状性颅内出血的比例低于溶栓组,差异均具有统计学意义($P<0.05$);2组的二次栓塞比例差异无统计学意义($P>0.05$),见表4。

表2 2组治疗前后NIHSS评分比较情况(分, $\bar{x}\pm s$)

组别	例数	治疗前	治疗后24 h	治疗后3 d	治疗后7 d
溶栓组	41	18.8±8.1	12.9±8.4 ^①	8.1±3.8 ^①	5.4±2.3 ^①
取栓组	58	17.8±9.6	8.7±5.0 ^{①②}	6.1±3.6 ^{①②}	4.1±2.6 ^{①②}

注:与治疗前比较,^① $P<0.05$;与溶栓组比较,^② $P<0.05$

表3 2组治疗7 d后的疗效比较[例(%)]

组别	例数	基本治愈	显效	有效	无效	总有效
溶栓组	41	13(31.7)	18(43.9)	5(12.2)	5(12.2)	36(87.8)
取栓组	58	29(50.0) ^①	24(41.4)	3(5.17)	2(3.45) ^①	57(96.6) ^①

注:与溶栓组比较,^① $P<0.05$

表4 2组不良事件发生比例[例(%)]

组别	例数	二次栓塞	颅内出血	症状性颅内出血
溶栓组	41	2(4.88)	4(9.76)	2(4.88)
取栓组	58	5(8.62)	2(3.45) ^①	1(1.72) ^①

注:与溶栓组比较,^① $P<0.05$

3 讨论

临床常见的脑梗死一般位于大脑中动脉供血区域,一旦大脑中动脉主干栓塞,1 h内就形成不可逆转的梗死核心及可挽救的缺血半暗带,短时间内恢复血流栓塞血管的血流,可显著减小梗死体积,改善患者的临床预后^[7]。国外多项统计显示,脑缺血发生6 h内恢复血流,可显著减小梗死体积,且越早恢复血流,临床

预后越好,所以急性大脑中动脉脑梗死发生后应尽早恢复梗死区域的血流^[8]。目前对脑梗死确切有效的治疗方式有静脉溶栓、选择性动脉溶栓治疗和支架取栓治疗。静脉溶栓是一种安全、有效,且对技术要求相对较低的治疗方法,但是其发病时间必须小于4.5 h,否则容易引发颅内出血的并发症,加重患者病情^[2]。对于发病时间超过4.5 h的患者,临床一般采用药物保守治疗和介入治疗,介入治疗主要为选择性动脉溶栓治疗和支架取栓治疗。选择性动脉溶栓治疗是将溶栓药物通过微导管注入栓塞部位,直接将血栓溶解,恢复闭塞血管的血流,改善微循环,挽救缺血半暗带,减小梗死体积^[9]。但动脉溶栓是一把双刃剑,取得良好临床效果的同时需要承担局部高浓度溶栓药物引起的颅内出血的风险,另外有些血栓为陈旧性血栓,单纯的动脉溶栓不能溶解血栓,耽误病情,影响患者的临床预后。

近年来,随着介入技术的进一步发展,血管内支架机械取栓治疗颅内大动脉急性栓塞越来越受到关注,成为治疗脑大动脉闭塞常用的治疗方法之一。动脉取栓是采用物理方式将血栓从动脉血管中取出。支架取栓对迅速开通闭塞大血管、恢复血流有无法替代的优势,已成为目前治疗急性缺血性卒中的重要选择和研究热点。支架机械取栓是通过支架拉栓的方式直接将堵塞血管的栓子取出,实现缺血区域的血流再灌,提高患者的短期和长期预后^[10]。目前常用的机械取栓装置有Merci取栓装置、Penumbra取栓装置和Solitaire取栓系统等。国内外多项临床研究显示Solitaire支架取栓系统的血管开通率可达到90%以上,且治疗时间短,手术并发症低,目前是临床上应用最广泛、治疗效果最好的颅内血管取栓装置^[11]。2015年,多项临床研究提示急性脑梗死患者及时给予支架取栓治疗,可显著改善患者90 d的临床效果,降低患者30 d内的死亡率和症状性脑出血的发生率,其治疗效果优于单纯溶栓治疗,并建议介入医生对发病8 h内的前循环动脉急性闭塞性卒中患者积极给予机械取栓治疗^[12,13]。该项研究近期的研究结果表明支架取栓治疗同样可改善患者的长期预后,降低患者再发脑梗死的风险^[14]。

通过对选择性动脉溶栓和支架取栓的2组患者对比分析,本研究发现支架机械取栓具有一定优势,可更

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快地恢复患者血流,且血管再通的比例增高,对患者的长期预后也有良好的效果,且有效降低患者治疗过程中的不良事件发生,对临床治疗具有指导意义。

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