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· 综述与讲座 ·

直接抽吸首次通过技术用于急性缺血性卒中的研究进展

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[摘要]　直接抽吸首次通过技术(ADAPT)是采用抽吸导管直接抽吸取栓实现血管再通的取栓方式,ADAPT 取栓快捷、安全、有效,是不劣于支架取栓的血管内治疗新策略,并被写入临床指南,是大血管闭塞性急性缺血性卒中机械取栓的一级推荐疗法。然而,国内部分神经介入医师对 ADAPT 的认识尚不充分,在临床实际应用中仍以支架取栓为主。ADAPT 操作简便,但影响因素众多,支持导管的选择、抽吸导管的口径、抽吸方式、闭塞血管的位置以及血栓性质、患者年龄、就诊时间等均可能影响抽吸取栓的效果。

[关键词]　缺血性卒中;　大血管闭塞性卒中;　直接抽吸;　机械取栓;　血管内治疗
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静脉溶栓是急性缺血性卒中(AIS)的一线标准疗法,然而对大血管闭塞性 AIS(LVO-AIS)患者,静脉溶栓再通率低,临床预后差。研究证实早期实现成功再灌注可降低大血管闭塞性 AIS 患者的死亡率,改善临床及功能预后[1-2]。支架取栓被证实是 LVO-AIS 患者血管内治疗实现成功再灌注的有效方法[3-4]。抽吸取栓是实现再灌注的另一种方法,直接抽吸首次通过技术(ADAPT)是用大口径抽吸导管直接抽吸取栓。近年来,抽吸取栓发展迅速,多项研究证实 ADAPT 是不劣于支架取栓的血管内治疗新选择[5]。ADAPT 以其更高的再通率、更短的手术时间、更低的经济成本等,受到国际神经介入医师的广泛认可[6-7]。但是 ADAPT 在国内卒中中心的使用率并不高[8]。本文将结合国内外研究进行分析总结,探讨 ADAPT 的疗效及相关影响因素。

一、抽吸取栓技术发展演变情况

抽吸取栓并不是一项新技术,2002 年 Lutsep 等[9]报道了 3 例颈动脉闭塞患者,7F 长鞘到达血栓近端,60ml 注射器进行抽吸取栓,3 个月后 2 例患者功能恢复良好。同年,Chapot 等[10]报道了 2 例使用 4F/5F 导管 +50ml 注射器完成基底动脉尖血栓抽吸的患者,其中 1 例获得良好预后。2005 年,Xu 等[11]报道了 2 例使用 8F 指引导管 +50ml 注射器完成颈动脉窦部血栓抽吸的病例,均获得成功再通。2006 年,Imai 等[12]报道了 14 例采用碎栓及抽吸的方式进行机械取栓(MT)的患者,其中 7 例获得了完全或部分再通,6 例获得良好预后。2008 年,关于 Penumbra System(PS)的前瞻性研究对 23 例患者进行血栓清除术,经指引导管送入再灌注导管到达栓塞部位,然后使用抽吸泵进行抽吸取栓,如果抽吸后仍有血栓残留,则使用血栓清除环取栓,最终 23 例患者全部实现了血管再通[13]。2009 年,另一项评价 PS 的多中心前瞻性研究纳入 125 例患者进行抽吸取栓,其中 82% 实现成功再通[14]。2010 年,Kang 等[15]对 PS 进行改良,提出 FAST(Forced Aspiration Suction Thrombectomy)技术,采用该技术的 22 例患者均实现完全再通,45% 实现 3 个月功能独立。2012 年开启的 THERAPY 试验对比了静脉溶栓后桥接抽吸取栓与单纯静脉溶栓的疗效,该试验因 5 大随机对照试验(RCT)结果证实,血管内治疗比单纯药物治疗 LVO-AIS 更有效而提前终止,最终纳入 108 例患者,55 例采用阿替普酶(tPA)静脉溶栓后 PS 抽吸取栓,53 例只进行 tPA 静脉溶栓,主要终点事件为 90 天功能良好[改良 Rankin 评分量表(mRS)评分 0 ~2 分],桥接抽吸取栓组和单纯静脉溶栓组患者 90 天功能良好比率分别为 38.0% 和 30.4%[16]。2014 年 Turk 等[5,19]在 ADAPT FAST study 研究中首次提出 ADAPT,采用大口径抽吸导管进行抽吸取栓,共纳入 98 例患者,其中 78% 单用 ADAPT 实现成功再通[改良脑梗死溶栓治疗(mTICI)≥2b 级],总体再灌注率为 95%。随后几年,随着抽吸导管的发展,ADAPT 也有了进一步提高,并逐渐成为 LVO-AIS 患者 MT 的一级推荐方案[23]。

二、ADAPT 操作步骤

ADAPT 是通过接触抽吸实现血管再通的方法。Turk 教授对 ADAPT 进行了详细描述,操作过程中指引导管(或长鞘及球囊导管等)提供支撑及稳定性,在前循环,指引导管头端推进到颈内动脉颅底或岩骨段,在后循环,指引导管头端推进到较粗椎动脉的 V2 段,根据闭塞血管直径,选择闭塞血管可容纳的最大口径抽吸导管。用于大脑中动脉 M1 段、颈内动脉末端或基底动脉闭塞的通常为内径 0.054 英寸、0.060 英寸、0.064 英寸或 0.068 英寸抽吸导管,如 5MAX、ACE060、ACE064、ACE068 等。在路线图引导下,在微导丝和微导管的支撑及引导下将抽吸导管安全推送至血栓水平,抽吸导管、微导管和微导丝构成三轴系统,该系统几乎可通过任何虹吸段弯曲和眼动脉弯曲[5]。随着抽吸导管性能的提升,有些抽吸导管可在没有微导丝及微导管引导下顺利到达栓塞部位[17]。为了尽可能的减少血栓的裂解而增加血栓逃逸引起远端血管栓塞的风险,微导管通常不穿越血栓,抽吸导管头端接近血栓后,抽吸导管尾端链接专用 Penumbra 抽吸泵或者 20 ~60 ml 注射器,打开负压即可进行抽吸,抽吸前撤出微导管及微导丝可以增加抽吸血流[18]。抽吸时如无逆向血流或血流缓慢呈滴状,提示抽吸导管头端接近并吸附血栓,此时导管再稍微向前推进 1 ~2mm,以接近血栓核心部位,此时逆向血流停止,提示血栓嵌顿在导管头端或吸入抽吸导管内,然后缓慢回撤抽吸导管,同时指引导管的尾端侧孔也保持负压抽吸。如果一次抽吸后未实现再灌注,可以将抽吸导管快速送到栓塞部位,以同样的方法进行再次抽吸,术者也可根据临床经验,经该系统送入取栓支架进行补救[5,19]。

三、影响抽吸效果的因素

1. 近端支持导管

近端支持导管是 ADAPT 成功建立通路的基础,为整个抽吸系统提供支撑力和稳定性,不同的支持导管可能会影响中间导管的通过性及达到栓塞部位靠近血栓近端的能力,进而影响抽吸成败[20]。常用的近端支持导管有长鞘、球囊导管或指引导管。NeuronMAX088

长鞘在多项实验研究中均有应用，也是目前 MT 中应用最多的近端支持导管之一[19,21-22]。球囊导管在抽吸取栓也中经常使用，有研究表明，使用球囊导管可以阻断近端血流，减少血栓逃逸远端栓塞风险，减少取栓次数，缩短的手术时间，提高首次再通率[24-25]。其他可用的指引导管有 Envoy、Cook Shuttle、Guider Softip XF、Northstar、Match1、普微森等，术中需结合患者的血管解剖结构、导管的兼容性等因素综合考虑，选择合适的近端支持导管。

2. 抽吸导管

抽吸导管性能的提升促进了 ADAPT 的发展。抽吸导管的内径是影响抽吸成功率的重要因素，其内径越大，产生的抽吸力越大，抽吸取栓成功率也越高。与 ACE60 抽吸导管相比，使用 ACE68 抽吸导管再通率更高，手术时间更短[26-27]。抽吸导管内径与栓塞部位近端血管内径比值也是影响抽吸成功率的因素，比值越大，抽吸成功率越高[28-29]。同样，0.072英寸内径抽吸导管较小口径抽吸导管有更高的再通率及更短的手术时间[30-31]。目前最大口径的抽吸导管是 0.088 英寸，其在体外模拟抽吸取栓实验中的首次再通率明显高于其他抽吸导管[32-33]。抽吸导管头端的斜面设计能提高抽吸效果，有报道 0.088 英寸的斜面头端抽吸导管在 MI 和 M2 段闭塞的卒中患者抽吸取栓是安全有效的[34]。

3. 抽吸方式

抽吸方式有抽吸泵持续压力抽吸、抽吸泵循环压力抽吸、20 ~ 60 ml 注射器手动抽吸。在体外实验中 60ml 注射器产生的真空压力高于自动抽吸泵，实际操作中注射器手动抽吸安全有效，经济成本更低[35-36]。在体外模型比较中，抽吸泵循环压力抽吸的清除率及抽吸效率均优于恒定压力抽吸[37]。但在实际工临床作中，哪种抽吸方式预后更好还需要更多的 RCT 进一步验证。

4. 闭塞部位及血栓与抽吸导管接触角度

血管闭塞的位置与抽吸再通成功率相关。研究表明，相比颈内动脉虹吸段闭塞或串联病变，孤立大脑中动脉闭塞是抽吸取栓成功再通有利因素[38]。抽吸导管头端与血栓接触的夹角（AOI）也是影响抽吸效果的重要因素，其 AOI 越大抽吸效果越好，可能原因是抽吸导管与血栓之间的 AOI 越小，摩擦力越大，阻碍血栓吸入导管内。AOI≥122.5°是大脑中动脉能否采取 ADAPT 技术实现再通的预测指标[39]。

5. 血栓性质

相关研究结果表明，血栓成分影响抽吸成功率，富含红细胞的血栓支架取栓的成功率更高，可能是因为这种血栓通常为新鲜的，质地较软，容易与取栓支架融合，相比之下，富含纤维蛋白的血栓 ADAPT 取栓成功率更高[40]。

6. 患者相关因素

患者越年轻，发病至手术时间越短，抽吸取栓再通可能性越大[38,41]。前者可能原因是年轻患者血管状况好，严重迂曲及狭窄病变少，易于建立通路，抽吸导管容易达到预期位置；后者可能原因是随着时间的延长，血栓与血管壁发生作用，黏附牢固[42]。

四、ADAPT在急性前循环大血管闭塞性卒中的应用

对于急性前循环大血管闭塞性卒中，ADAPT 抽吸取栓安全有效，不劣于支架取栓，且经济成本更低。目前 ADAPT 取栓的 RCT 研究（ASTER、COMPASS）都是基于前循环大血管闭塞的，在 ASTER 研究中，ADAPT 术后再灌注率与支架取栓术后再灌注率分别为 85.4% 和 83.1%，在 24 小时的美国国立卫生研究院卒中量表评分（NIHSS）变化、90 天的 mRS 评分和不良事件方面，ADAPT 与支架取栓之间比较均没有显著差异[43]。在 COMPASS 研究中，主要研究结果为 90 天良好功能预后（mRS 评分 0 ~ 2 分），抽吸组 69 例（52%）在 90 天时获得良好功能预后，支架取栓组 67 例（50%）在 90 天时获得良好功能预后，而在颅内出血、全因死亡率方面二者比较均无明显差异[21]。多项回顾性观察研究也得出类似结论，ADAPT 取栓从穿刺到再灌注时间更短。Lapergue 等[44]回顾性分析了 243 例急性前循环大血管闭塞性卒中患者发病 6 小时内接受 MT 治疗，124 例接受 ADAPT 取栓，119 例接受 Solitaire 支架取栓，接受 ADAPT 治疗的患者再灌注率更高（82.3% 比 68.9%，P = 0.022）。在临床结局、并发症及远端栓塞、无症状性颅内出血等方面两组比较均无显著差异，ADAPT 组从穿刺到血管再通时间略短（45 分钟比 50 分钟，P = 0.42）。Martini 等[45]进行了一项多中心国际性回顾性研究，纳入了来自北美 15 家卒中中心的大血管闭塞性脑梗死患者，排除后循环梗死，107 例接受直接抽吸术取栓治疗，121 例接受支架取栓治疗，两组患者 90 天功能预后相似，90 天 mRS 评分均为（3.0 ± 2.4）分，术后再灌注率比较也无明显差异，抽吸组略高（91.2% 比 87.5%）。Stapleton 等[46]进行的观察性研究也显示出类似结论，该研究纳入 117 例急性前循环大血管闭塞性卒中患者，47 例采用 ADAPT 取栓，70 例采用支架取栓；结果显示，ADAPT 组和支架组患者术后再灌注率相似（82.9% 比 71.4%，P = 0.19），90 天良好功能预后（mRS 评分 0 ~ 2 分）比率相似（48.9% 比 41.4%，P = 0.45），ADAPT 组手术时间更短（54.0 分钟比 77.1 分钟，P <

0.01),在颅内出血及手术相关并发症方面两组之间比较均没有明显差异。多项 Meta 分析也显示在急性前循环大血管闭塞性卒中患者中,ADAPT 安全有效。Gory 等[47]对 16 篇文献中的 1 378 例采用 ADAPT 取栓的急性前循环大血管闭塞性卒中患者进行 Meta 分析,结果显示首次成功再通率为 66%,支架补救率为 31%,最终再通率为 89%,90 天功能良好率为 50%,90 天内的死亡率为 15%,症状性颅内出血为 5%。Boulanger 等[48]分析了 15 项研究的 1 817 例患者,直接抽吸取栓的最终成功再通率(mTICI≥2b 级)相比支架取栓略高(87.9% 比 71.3%,$P<0.001$),直接抽吸取栓与支架取栓的最终完全再灌注率(mTICI 3 级)比较没有显著差异(51.1% 比 38.3%,$P=0.150$),直接抽吸取栓与支架取栓的 90 天功能良好率比较无显著差异(45.0% 比 52.4%,$P=0.450$)。整体而言,ADAPT 在急性前循环大血管闭塞性卒中的应用安全有效,其再灌注率、90 天功能预后等与支架取栓比较无明显差异,颅内出血、远端栓塞、手术相关并发症、全因死亡率等与支架取栓比较也无明显差异,直接抽吸取栓从穿刺直再灌注时间更短,器材相关花费更低,是值得推荐的一线血管内治疗策略。

五、ADAPT 在后循环 AIS 的应用

目前尚无基底动脉闭塞脑梗死支架取栓与 ADAPT 取栓对比的前瞻性 RCT 研究。但是,多项观察性研究及 Meta 分析结果表明,对急性基底动脉闭塞性卒中,ADAPT 取栓可获得更高的再灌注率及更短时手术时间,抽吸取栓与支架在 90 天功能预后、并发症发生率、全因死亡率等发面比较无显著差异[49-54]。

六、ADAPT 在中远段血管闭塞中的应用

观察性研究及 Meta 分析结果表明,对于中远段血管(M2 远端及 M3)闭塞性卒中,ADAPT 取栓成功再通率及功能独立率均低于支架取栓[56-57],尚需要 RCT 研究进一步探讨中远段血管闭塞性卒中的最佳疗法。

综上所述,ADAPT 是 AIS 血管内治疗的有效手段,是与支架取栓相媲美的再灌注策略。实际工作中,神经介入医师要结合患者的病史及脑血管造影实时情况,选择合适的支持导管及抽吸导管、恰当抽吸方式、转换策略与补救措施,以提高再灌注率,缩短发病至再灌注时间,减少并发症,从而改善患者预后。

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