

·综述 General review·

机械取栓术后无效复流的影响因素研究进展

刘 肖, 周腾飞, 李天晓

【摘要】 机械取栓可以改善急性前循环大血管闭塞性卒中临床预后, 然而一部分患者虽然实现了成功再通, 但无效复流并未使患者获得良好预后。影响无效复流的因素很多, 本文对影响前循环大血管闭塞机械取栓术后无效复流的因素, 如年龄、再通时间、梗塞体积、基线严重程度、血压等进行综合叙述分析。

【关键词】 急性脑卒中; 机械取栓; 无效复流; 预测因素; 预后

中图分类号: R743.3 文献标志码: A 文章编号: 1008-794X(2024)-03-0321-04

Progress in the research on the influencing factors of futile recanalization after mechanical thrombectomy

LIU Xiao, ZHOU Tengfei, LI Tianxiao. Henan Provincial People's Hospital, Zhengzhou, Henan Province 450003, China

Corresponding author: LI Tianxiao, E-mail: dr.litianxiao@vip.163.com

【Abstract】 Mechanical thrombectomy can improve the clinical outcome of patients with acute anterior circulation larger vessel occlusive stroke. However, a remarkable proportion of patients, even they have achieved a successful recanalization, still develop adverse outcomes, such as futile recanalization (FR). According to relevant literature reports, there are many factors that can affect futile recanalization. In this paper, a series of factors such as age, recanalization time, infarct volume, baseline severity, blood pressure that may affect futile recanalization of mechanical thrombectomy in patients with in anterior circulation large vessel occlusion will be comprehensively described and analyzed. (J Intervent Radiol, 2024, 33: 321-324)

【Key words】 acute stroke; mechanical thrombectomy; futile recanalization; predictive factor; prognosis

目前,机械取栓已成为救治急性大血管闭塞性卒中的首选方案,大血管闭塞导致的急性缺血性卒中接受取栓治疗的成功再通率大幅度提升。一项荟萃分析显示,接受以取栓支架为主的治疗可以实现71%的成功再通率($mTICI \geq 2b/3$),但是患者的整体良好预后仍然处于较低水平,近一半的患者面临无效复流^[1]。无效复流是指血管虽然实现了成功再通,仍然未获得良好的预后。影响无效复流的因素很多,本文对影响机械取栓无效复流的相关因素,如年龄、再通时间、梗塞体积、基线严重程度、血压等进行综合叙述分析。

1 无效复流的发生机制

机械取栓术后,当核心梗死体积较大、可挽救的缺血半暗带体积较小,梗死部分处于失代偿期,再通往往会导致无效复流,即便影像学提示为可挽

救半暗带的组织,实际再灌注后依然可能会发展为不可逆梗死,从而导致无效复流的发生。研究显示,脑血流自动调节能力的损伤会增加无效复流的发生,中重度脑组织缺血会导致患者脑血流自动调节能力的损伤^[2],从而容易引起再灌注后出现高灌注、脑水肿等现象,治疗中使用的溶栓药物 rtPA 也对脑血流自动调节能力产生一定的影响^[3]。脑组织再灌注损伤的原因主要包括自由基过度形成、兴奋性氨基酸毒性作用、细胞内钙超载和炎症反应等,这些因素互相影响,进一步促进脑缺血再灌注损伤后的神经功能破坏,使缺血半暗带的脑组织缺血坏死而不可逆转,即发生再灌注损伤,再灌注损伤将导致脑血流无效复流的发生^[4]。还有研究提示,微循环损伤也是无效灌注发生的机制之一,梗塞后发生的一系列炎症反应以及免疫反应,比如血小板和细胞的激活等,可能会出现毛细血管循环障碍,影响脑组

织再灌注导致无效复流。脑血管成功再通后,早期再闭塞常发生于术后的数小时内,患者早期神经功能恶化,导致机械再通无效复流^[5]。

2 无效复流的相关预测因素

2.1 年龄

研究证实,年龄是再通后无效复流的独立预测因子^[67]。老年患者经常被排除在随机对照试验之外,虽然与传统的保守治疗或静脉溶栓相比,老年患者也可能受益于血管内治疗,机械取栓甚至可能为90岁以上的人提供实质性的益处。与年轻患者相比,80岁以上接受血管内治疗的患者表现出较低的临床转归率和较高的病死率^[8-9]。随着年龄的增加卒中的发生率增加,接受大血管闭塞取栓治疗的高龄患者占很大一部分,然而这些患者基础疾病较多,特别是接受全身麻醉治疗时其围手术期并发症相应增加,随着年龄的增长神经可塑性下降,即便是成功灌注,神经功能的恢复能力有限。另外,随着年龄的增长,脑组织合并一些变化如脑白质疏松、血脑屏障脆弱,这些因素将增加高龄患者再通后出血转化风险。

2.2 再通时间

脑卒中的救治强调时间就是大脑,虽然目前机械取栓救治发病至再通时间窗延长到24 h,但是时间依然是患者再通治疗中影响预后的重要因素。随着发病至再通时间的延长,脑组织将发生不可逆的死亡。既往研究证实,发病至再通时间是影响再通无效复流的一个重要因素^[10-11]。一项荟萃分析显示,1 000例患者每缩短15 min再通时间,将有39例患者减轻致残风险,其中25例患者实现良好预后。除了发病至再通时间,机械取栓手术操作时间也可能影响患者的无效复流,手术操作时间往往与手术操作难度有关,手术操作时间延长往往预示血管路径迂曲、取栓次数较多、血栓负荷量较大等,较长时间的操作也进一步加重血管损伤,从而增加无效复流^[12]。

2.3 NIHSS 评分

相对于低评分患者,即便是获得成功再通的情况下,高NIHSS评分的无效再通复流的比例较高^[12]。Lee等^[13]对影响无效复流因素进行分析,结果显示NIHSS评分<5分的患者无效复流的比例为21%,11~20分的无效复流比例为59%,NIHSS评分>20分的患者无效复流比例为64%。另有研究显示,NIHSS评分>20分的患者,无效复流比例达到了66%^[14]。对于症状较重的患者,往往梗塞范围

较大,梗死核心较大,部分患者即便成功再通,依然难以挽救核心梗死区域。随着术前NIHSS评分增加,患者无效复流比例也增加,但相比于药物治疗,血管内再通治疗依然能够使术前NIHSS较高的患者获益。

2.4 影像预测因子

术前影像学检查可以体现患者无效复流的预测因素。梗塞范围、侧支循环、血栓负荷量等都与机械取栓再通复流后不良预后有关。术前梗塞范围大小与患者再通治疗临床预后显著相关,相比于ASPECT评分较高的患者,评分较低的患者难以从血管内再通治疗中获益^[15]。基于CTA源性的ASPECT评分研究也显示,较低的评分与再通后无效复流显著相关^[16]。再通后短期内梗塞体积的大小往往预测最终梗死体积,与患者临床预后显著相关^[17]。再通后梗死体积较大时,也是机械再通无效复流的预测因素^[18]。术前侧支循环的评分也与患者预后存在相关性,侧支循环是缺血半暗带存在的结构基础,良好的侧支循环预示有较好的代偿及较多的可挽救组织,侧支循环较差时,患者再通后无效复流将增加。既往研究指出,基于ASL成像或CTA成像的侧支循环评估提示,较差的侧支循环与患者再通治疗后不良预后相关^[19-20]。随着血栓负荷量的增加,患者可能受损的脑灌注区域也增加,同时取栓的难度、取栓的时间将相应增加,使患者接受机械取栓后无效复流的比例随之增加^[21]。

2.5 血流再通程度

虽然取栓后血流达到TICI2b以上均称为成功再通,但是手术后不同再通程度与患者预后存在差异。在HERMES的回顾性分析中,无残疾或轻度残疾(mRS 0-1)受试者比例的增加与较高的eTICI血流分级具有显著相关性^[22]。与TICI2b相比,TICI3级血运重建有较高的良好功能预后率、较低的病死率和颅内出血发生率^[23]。血流再通不全的原因包括残余血栓迁移、靶血管狭窄、远端栓塞等,可能导致低灌注、新区域梗死以及脑卒中复发,这些因素都可能增加无效再通的风险。

2.6 围术期血压

急性缺血性脑卒中发病早期可出现反应性血压升高,可促进脑灌注,有研究提示术前较高的血压是患者无效复流的预测因素。缺血性卒中患者的基线收缩压(SBP)水平越高,其良好功能预后的可能性越低,无效复流的比例将增加^[24]。在血管再通成功后,血压升高可增加高灌注,加重脑水肿,进而影

响血流,尤其是大面积缺血性患者,过度灌注梗死扩大,导致不良预后。既往研究表明,再通术后高血压与颅内出血之间也存在相关性^[25]。最新研究 Enchanted 2 结果显示,术后标准降压组(140~180 mmHg)与强化降压组(<120 mmHg)比较,强化降压组 90 d 内早期神经功能恶化($OR=1.53, 95\%CI: 1.18\sim1.97$)和严重残疾($OR=2.07, 95\%CI: 1.47\sim2.93$)风险更高,但两组在症状性脑出血、病死率或严重不良事件方面差异无统计学意义^[26]。另有研究显示,较高的血压变异波动与患者预后存在相关性^[27]。

2.7 其他预测因素

性别也是无效复流的影响因素。女性比男性的无效复流比例高,这可能是因为女性患者高龄、心源性栓塞的比例更高^[28]。麻醉方式也可能是影响患者不良预后的因素,有研究显示全身麻醉更容易导致无效复流^[12]。另外,糖尿病病史、闭塞部位以及取栓次数等都可能影响患者无效复流的发生^[29-30]。取栓术后出现出血转化或者明显的脑水肿,也预示着无效复流的发生^[31]。无效复流的发生有时候不由一种因素决定,为了提高预测准确性,提出了多因素组合预测评分,如综合了 NIHSS 评分、年龄以及 PER 评分可以更好地预测患者无效复流的发生^[32]。

3 无效复流的预防

提高机械取栓的良好预后、降低无效复流的发生是临床一项重要挑战。首先在筛选患者方面,纳入多个因素如年龄、影像学表现、症状等进行综合分析,有助于规避可能发生无效复流的患者,筛选出可能获益的患者;其次在手术操作方面,优化取栓工具,提高取栓技术,尽可能一次实现完全再通、实现快速再通,这样可以缩短再通时间,减少术中并发症,提高良好预后比例;最后对于术后患者,通过严格的围术期管理,最大程度降低患者无效复流的发生。

[参考文献]

- [1] Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials[J]. Lancet, 2016, 387: 1723-1731.
- [2] Tian G, Ji Z, Huang K, et al. Dynamic cerebral autoregulation is an Independent outcome predictor of acute ischemic stroke after endovascular therapy[J]. BMC Neurol, 2020, 20: 189.
- [3] Reinhard M, Wihler C, Roth M, et al. Cerebral autoregulation dynamics in acute ischemic stroke after rtPA thrombolysis[J]. Cerebrovasc Dis, 2008, 26: 147-155.
- [4] Haussen DC, Nogueira RG, Elhamady MS, et al. Infarct growth despite full reperfusion in endovascular therapy for acute ischemic stroke[J]. J Neurointerv Surg, 2016, 8: 117-121.
- [5] Qureshi AI, Hussein HM, Abdelmoula M, et al. Subacute recanalization and reocclusion in patients with acute ischemic stroke following endovascular treatment[J]. Neurocrit Care, 2009, 10: 195-203.
- [6] Zhou T, Yi T, Li T, et al. Predictors of futile recanalization in patients undergoing endovascular treatment in the DIRECT-MT trial[J]. J Neurointerv Surg, 2022, 14: 752-755.
- [7] 孟飞龙,徐浩文,权涛,等.急性颅内大血管闭塞机械再通患者预后影响因素分析[J].介入放射学杂志,2020,29:1177-1181.
- [8] Khan MA, Baird GL, Miller D, et al. Endovascular treatment of acute ischemic stroke in nonagenarians compared with younger patients in a multicenter cohort[J]. J Neurointerv Surg, 2017, 9: 727-731.
- [9] Hwang K, Hwang G, Kwon OK, et al. Endovascular treatment for acute ischemic stroke patients over 80 years of age[J]. J Cerebrovasc Endovasc Neurosurg, 2015, 17:173-179.
- [10] Saver JL, Goyal M, van der Lugt A, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis[J]. JAMA, 2016, 316: 1279-1288.
- [11] Khatri P, Yeatts SD, Mazighi M, et al. Time to angiographic reperfusion and clinical outcome after acute ischaemic stroke: an analysis of data from the Interventional Management of Stroke (IMS III) phase 3 trial[J]. Lancet Neurol, 2014, 13: 567-574.
- [12] Xu H, Jia B, Huo X, et al. Predictors of futile recanalization after endovascular treatment in patients with acute ischemic stroke in a multicenter registry study[J]. J Stroke Cerebrovasc Dis, 2020, 29: 105067.
- [13] Lee SH, Kim BJ, Han MK, et al. Futile reperfusion and predicted therapeutic benefits after successful endovascular treatment according to initial stroke severity[J]. BMC Neurol, 2019, 19: 11.
- [14] Shi ZS, Liebeskind DS, Xiang B, et al. Predictors of functional dependence despite successful revascularization in large-vessel occlusion strokes[J]. Stroke, 2014, 45: 1977-1984.
- [15] Espinosa de Rueda M, Parrilla G, Manzano-Fernandez S, et al. Combined multimodal computed tomography score correlates with futile recanalization after thrombectomy in patients with acute stroke[J]. Stroke, 2015, 46: 2517-2522.
- [16] Kawiorski MM, Martínez-Sánchez P, García-Pastor A, et al. Alberta stroke program early CT score applied to CT angiography source images is a strong predictor of futile recanalization in acute ischemic stroke[J]. Neuroradiology, 2016, 58: 487-493.
- [17] Boers AMM, Jansen IGH, Beenen LFM, et al. Association of follow-up infarct volume with functional outcome in acute ischemic stroke: a pooled analysis of seven randomized trials[J]. J Neurointerv Surg, 2018, 10: 1137-1142.

- [18] Zaidi SF, Aghaebrahim A, Urrea X, et al. Final infarct volume is a stronger predictor of outcome than recanalization in patients with proximal middle cerebral artery occlusion treated with endovascular therapy[J]. *Stroke*, 2012, 43: 3238-3244.
- [19] 徐志嘉, 曹月洲, 赵林波, 等. 基于机械取栓术前 CTA 的侧支循环评分对动脉粥样硬化狭窄型急性大脑中动脉闭塞的预测价值[J]. *介入放射学杂志*, 2023, 32: 114-118.
- [20] Liu S, Fan D, Zang F, et al. Collateral circulation detected by arterial spin labeling predicts outcome in acute ischemic stroke [J]. *Acta Neurol Scand*, 2022, 146: 635-642.
- [21] Derraz I, Pou M, Labreuche J, et al. Clot burden score and collateral status and their impact on functional outcome in acute ischemic stroke[J]. *AJNR Am J Neuroradiol*, 2021, 42: 42-48.
- [22] Liebeskind DS, Bracard S, Guillemin F, et al. eTICI reperfusion: defining success in endovascular stroke therapy[J]. *J Neurointerv Surg*, 2019, 11: 433-438.
- [23] Rizvi A, Seyedsaadat SM, Murad MH, et al. Redefining 'success': a systematic review and meta-analysis comparing outcomes between incomplete and complete revascularization[J]. *J Neurointerv Surg*, 2019, 11: 9-13.
- [24] Goyal N, Tsivgoulis G, Iftikhar S, et al. Admission systolic blood pressure and outcomes in large vessel occlusion strokes treated with endovascular treatment[J]. *J Neurointerv Surg*, 2017, 9: 451-454.
- [25] Nogueira RG, Liebeskind DS, Sung G, et al. Predictors of good clinical outcomes, mortality, and successful revascularization in patients with acute ischemic stroke undergoing thrombectomy: pooled analysis of the Mechanical Embolus Removal in Cerebral Ischemia(MERCI) and Multi MERCI Trials[J]. *Stroke*, 2009, 40: 3777-3783.
- [26] Yang P, Song L, Zhang Y, et al. Intensive blood pressure control after endovascular thrombectomy for acute ischaemic stroke(ENCHANTED2/MT): a multicentre, open-label, blinded-endpoint, randomised controlled trial [J]. *Lancet*, 2022, 400: 1585-1596.
- [27] Goyal N, Tsivgoulis G, Pandhi A, et al. Blood pressure levels post mechanical thrombectomy and outcomes in large vessel occlusion strokes[J]. *Neurology*, 2017, 89: 540-547.
- [28] Hussein HM, Saleem MA, Qureshi AI. Rates and predictors of futile recanalization in patients undergoing endovascular treatment in a multicenter clinical trial[J]. *Neuroradiology*, 2018, 60: 557-563.
- [29] Rabinstein AA, Albers GW, Brinjikji W, et al. Factors that may contribute to poor outcome despite good reperfusion after acute endovascular stroke therapy[J]. *Int J Stroke*, 2019, 14: 23-31.
- [30] Baek JH, Kim BM, Heo JH, et al. Number of stent retriever passes associated with futile recanalization in acute stroke[J]. *Stroke*, 2018, 49: 2088-2095.
- [31] Ng FC, Yassi N, Sharma G, et al. Cerebral edema in patients with large hemispheric infarct undergoing reperfusion treatment: a HERMES meta-analysis[J]. *Stroke*, 2021, 52: 3450-3458.
- [32] Rangaraju S, Aghaebrahim A, Streib C, et al. Pittsburgh response to endovascular therapy(PRE) score: optimizing patient selection for endovascular therapy for large vessel occlusion strokes[J]. *J Neurointerv Surg*, 2015, 7: 783-788.

(收稿日期:2023-02-08)

(本文编辑:新宇)