

急性缺血性脑卒中机械取栓术后血压调控策略的研究进展

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摘要

急性大血管闭塞是导致急性缺血性脑卒中患者遗留中重度残疾和死亡的最主要原因。近年来, 机械取栓技术已成为治疗急性大血管闭塞性缺血性脑卒中的主要治疗手段, 除了手术, 围术期的血压管理也可能影响患者功能预后, 特别是术后的血压管理是其中重要的可控因素之一。截止目前, 关于急性大血管闭塞机械取栓术后的血压调控方案, 尚未形成共识。本文对急性大血管闭塞性缺血性脑卒中患者机械取栓术后血压管理的相关内容进行了综述, 旨在为机械取栓术后的血压管理提供参考。

关键词

急性缺血性卒中, 大血管闭塞, 机械取栓, 血压

Research Progress of Blood Pressure Control Strategy after Mechanical Thrombectomy for Acute Ischemic Stroke

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Abstract

Acute large vessel occlusion is the most critical cause of residual moderate to severe disability and death in patients with acute ischemic stroke. In recent years, mechanical embolization techniques have become the mainstay of treatment for acute large vessel occlusive ischemic stroke. In addition to surgery, perioperative blood pressure management may also affect the functional prognosis of patients, making it one of the key controllable factors as there is no consensus on the protocol for blood pressure management after mechanical embolization in acute ischemic large vessel occlusive stroke. This article reviews blood pressure management strategies after mechanical embolization for acute large vessel occlusive ischemic stroke, intending to provide a reference for blood pressure management after mechanical embolization.

Keywords

Acute Ischemic Stroke, Large Vessel Occlusion, Mechanical Thrombectomy, Blood Pressure

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1. 引言

急性缺血性脑卒中(acute ischemic stroke, AIS)约占所有脑卒中类型的 70%~85% [1]。然而,在超过 1/3 的 AIS 中可以检测到大血管闭塞(large vessel occlusion, LVO)的存在[2] [3]。目前静脉注射重组组织型纤溶酶原激活剂虽然是开通闭塞血管的标准治疗方式之一,但是机械取栓(mechanical thrombectomy, MT)技术却具有更高的再通效率、更广的适应证等优点,已逐渐成为治疗 AIS 的重要手段[4]。现有研究表明大多数受影响动脉的血流动力学变化发生在闭塞血管再通后的前 10 天内,血流动力学恶化也与临床恶化和功能预后不良有关[5] [6] [7] [8] [9]。特别是较高收缩压(Systolic blood pressure, SBP)及收缩压变异性(Systolic blood pressure variability, SBPV)较大对成功血管再通(定义为 mTICI 在 2b 级或 3 级)患者的不利影响可能更为显著[10]-[15]。因此,积极探索急性大血管闭塞性缺血性卒中(Acute ischemic stroke with large vessel occlusion, AIS-LVO)患者 MT 术后的血压(Blood pressure, BP)管理策略至关重要,对改善患者预后具有重大意义。

2. 大血管闭塞后脑血流动力学改变

2.1. 脑血流自动调节障碍

脑血流自动调节(Cerebrovascular Autoregulation, CA)是人脑血管系统的一个关键特征,以确保在不断变化的生理条件下大脑的充分氧合和代谢[16]。即平均动脉压(mean arterial blood pressure)在 60~150 mmHg 范围内变化时,颅内血管可通过自身收缩或舒张作用使之能够保证脑组织所需的脑血流量[17] [18]。微小动脉构成了血管阻力的主要部分,且在机体肌源性及神经源性等调节机制的作用下,微小动脉会对血管的管径适当做出调整,从而维持动脉 BP 在一定的范围内变化[19]。由于与微小动脉相比,大动脉的管壁较厚及中膜平滑肌层较多,因此在对抗动脉 BP 变化的过程中,颅内大动脉管壁的收缩功能与舒张功能有可能更加重要。随后 Warnert 等[20]学者通过利用脉自旋标记 MRI 技术监测成人颅内血管顺应性,

证实了这一点。

有关研究表明,缺血性脑卒中会导致 CA 出现障碍[21] [22]。此时若 MAP 不在 CA 能力的范围内时,大脑会更容易受到全身 BP 或颅内压变化影响,导致进一步的缺血性损伤或出血性脑损伤。既往研究表明急性闭塞血管再通后会立即出现脑血流量的急剧增加,这可能是由于 CA 受损以及血管扩张物质的释放,从而导致脑过度灌流和继发性再灌注脑损伤[23] [24]。2020 年, Meyer 等[25]前瞻性的分析了 MT 成功后恢复组织灌注与 CA 之间的潜在相关性,提示脑血流灌注可能因 CA 受损而受到影响。另外,有研究显示当术后 SBP 超过 159 mmHg 会导致患者的临床神经功能恶化[6],而这种恶化的结果可能是由于 CA 受损导致的持续脑血管高灌流作用所致,故严格的术后 BP 管理也是至关重要的。

2.2. 侧枝循环

在 AIS-LVO 发生后,血栓远端的灌流压力下降导致压力梯度,逆行血流开始通过脑侧枝循环,从而获得足够的脑血流水平以维持半暗带的生存[26]。在这种情况下,BP 下降或局部肿块效应导致的组织压力增加可能导致侧支循环梯度的减弱并加剧缺血[27]。故脑侧支循环成为近些年来学者研究的焦点之一。既往多项研究均发现侧枝血流灌注是对卒中后梗死体积以及 HT 的强预测因子[27] [28]。2016 年,Stelle 等[29]学者纳入 51 名急性大脑前动脉近端闭塞的患者,结果发现侧枝循环分级与皮质梗死体积之间存在中度负相关。随后 Wu 等[30]纳入 72 例接受取栓术的急性基底动脉闭塞患者,结果提示卒中的病情程度与侧支循环的分级有关,与重度卒中相比,轻、中度卒中的术后 3 个月良好结局较高、围术期的并发症发生率和死亡率较低。除此之外,由于脑侧支循环在急性缺血性卒中良好结局中具有重要作用,有研究显示老年人、高尿酸血症和代谢综合征是软脑膜侧枝循环不良的独立预测因子[31]。遗传因素(p.Arg4810Lys 变异体)在侧枝循环形成的过程中也是扮演了重要的作用[32]。因此,了解侧枝循环建立的相关因素,有助于临床医师早期识别高危患者,改善患者的临床预后。

3. 大血管闭塞患者血管内治疗术前及术后血压改变与预后

3.1. 术前血压变化与预后

BP 升高在 AIS 患者中很常见,一项涉及超过 25 万名患者的研究表明,大约 25% 的患者 SBP > 140 mmHg [33]。2015 年,MR CLEAN 研究[34]的后处理分析结果也一致显示,基线 SBP 与不良功能结局之间呈 U 形关系,其中最佳 BP 值是 120 mmHg,且每超过 10 mmHg,出血的相对风险上升 21%。之后多项研究均提示了相似的结果,入院时 SBP 和脑卒中预后之间呈 U 型关系,较高或较低的基线 BP 都与不良预后有关[35] [36]。2020 年, Berg 等[37]开展的队列研究结果显示,在接受血管内治疗的 AIS 患者中,较高的入院 BP 与再灌注成功概率较低和临床结果较差相关。然而,一项关于 LVO 的长队列研究发现,对于再灌注不成功的患者,较高的基线 BP 与梗塞组织生长增加有关,血管闭塞或狭窄的卒中患者基线 BP 较高与侧支循环血流较好相关[38]。总而言之,若成功实现血管再通的患者,则极端的术前 BP 均会对患者的预后带来不利影响;而对未成功取得再通的患者,较高的基线 BP 可能是有益的。

3.2. 术后血压变化与预后

既往多项研究显示接受血管内治疗的 AIS 患者,术后反射性 SBP 升高可能与 LVO、侧支循环不良、再通机会不佳、大面积梗死等脑卒中程度有关[39] [40] [41]。然而,在患者接受血管内治疗术后,较高的 SBP 或较大的 BPV 与 MT 术后脑实质 HT 发生率增加和神经功能预后变差相关[10]-[15]。2015 年,一项荟萃分析纳入 77,299 例心脑血管疾病患者,结果显示对卒中患者的病死率及卒中风险具有很高的预测价值的指标是 SBPV,表现为 SBP 标准差每增高 1 mmHg,死亡率及卒中风险均发生不同程度升高[42]。Eva

等[43]研究显示较高的收缩压峰值独立地与较差的术后3个月改良 Rankin 分级和较高的出血性并发症发生率相关。Han 回顾性研究[44]分析了303例LVO患者接受血管内治疗成功再通后的24h和48h内的短期BPV较大与早期神经功能恶化显著相关,可能是临床结果的独立预测因子。Zhang等[45]学者纳入接受血管内治疗的72例AIS-LVO患者,结果提示术后SBPV较低与3个月时的良好结局有关,SBPV可能是AIS-LVO患者功能预后的新预测因子。2021年荟萃分析评估2010~2020年内的3520名接受MT的AIS患者,结果提示SBPV较低与术后3个月良好功能结局有关,而较高SBPV与症状性颅内出血和全因死亡率无关[46]。BEST研究[47]二次分析发现对于前循环卒中患者术后24h内,BPV较大与术后90天临床预后不良有关。Chang等研究显示在成功实现血管再通的患者中,降低BPV可能对改善患者临床结局有积极的影响[48]。因此,合理的控制术后的BP及BPV有助于改善患者的预后。

4. 术后血压调控

基于以上研究结果,伴随着MT治疗之后血管成功再通,术后BP的升高和(或)BPV较大会极大的增加AIS-LVO患者的脑实质出血率及临床预后不良的比例(mRS评分 > 2分),故术后BP的管理将是AIS临床研究的重点之一。一项来自2018年美国的调查报告指出,大多数接受血管内治疗术后脑血管实现再通的患者倾向于较低的BP水平,而对于未能实现血管成功再通的患者则保持相对较高的BP水平[49]。因此,为了减少症状性出血转化的发生率及改善卒中患者的临床预后,应当依据闭塞血管的再通情况进行严格的术后BP调控。

2015年,ESCAPE研究[50]显示对于闭塞血管成功实现再通的患者,将BP控制至正常水平即可;而未实现血管再通的,则将SBP目标定为150mmHg以上更安全。随后DAWN研究[51]也表明将术后24小时SBP控制在140mmHg以下,这个BP目标将会有效降低不良事件的发生。2018年,一项发表于Stroke的131家在线问卷调查报告显示:对于成功血管再通的患者,36%(n=21)的机构将SBP控制在120~139mmHg,21%(n=12)的机构将SBP控制在140~159mmHg,28%(n=16)的机构将SBP控制在 \leq 180mmHg范围内,而将SBP控制在120~139mmHg之间成为大多数机构的选择;而在再通不成功的AIS患者中,43%(n=25)的机构则会将SBP控制在180mmHg以下,只有10%(n=6)的机构将SBP \leq 220mmHg作为BP调控的目标[49]。之后Anadani等[52]分析比较了1091例AIS取栓患者,将术后SBP分为低收缩压组(<140mmHg)、中收缩压组(<160mmHg)、高收缩压组(<180mmHg)共三组,结果显示后者(高收缩压组)明显差于前两组(低、中两组)90天的临床预后。2019年,Cernik等[14]学者分析发现血管再通后24h内SBP值的显著降低与AIS患者术后3个月良好预后有关,当SBP中位数在140mmHg以下时,患者临床结局改善明显且3个月死亡率较低。2020年,Matusevicius等[10]表明在成功再通的AIS患者中,将SBP控制在110~119mmHg范围内时,患者术后90天良好功能预后及脑实质出血转化发生率较低。

近年来,由于MT之后再灌注损伤的发生率和预后不良率较高,关于AIS取栓术后再灌注防治策略越来越受到重视。2021年,法国BP-TARGET多中心研究[53]分析了MT术后个体化强效降压治疗24h对术后脑实质出血转化的影响,结果显示:对于血管成功再通者,与标准降压治疗组(SBP维持在130~185mmHg)相比,100~129mmHg的强化降压治疗组并未有效降低术后24h~36h的颅内出血转化率。今年由国内外联合发表的ENCHANTED2/MT前瞻性临床研究[54]纳入了AIS-LVO取栓术后成功再灌注(eTICI 2b/2c/3)的患者,结果显示,与标准降压组(140~180mmHg)相比,术后强化降压(收缩压 < 120mmHg)治疗可能导致90天良好功能预后(mRS 0~2分)比例的下降,且可能导致早期神经功能恶化和更高的90天残疾率,但两组间症状性出血转化率方面并无显著差异。虽然这项试验得到了较为满意的答案,但未来可能需要更多的大型前瞻性临床研究来验证这一结果。

基于前人的辛苦努力,美国AHA/ASA指南建议将AIS患者经MT治疗实现血管成功再通后24小时

内将 BP 保持在 180/105 mmHg 以下, 但该指南证据推荐等级较低[55]。如今, 国内最新指南[56]推荐 MT 术后成功血管再通的患者, BP 应控制在 140 mmHg 以下会更有助于减少症状性出血转化的发生; 对于未血管成功再通的患者 BP 应控制在正常 BP 之上或更高, 可能会更有利于脑侧枝循环代偿通路的建立和维持。但由于该指南未对术后 BP 管理的下限提出参考, 同时目前也缺乏相关的大型、随机对照、前瞻性临床研究来验证最佳的 BP 目标。为此本团队已开展了一项针对 AIS-LVO 患者经 MT 成功再通后实行血压管理的多中心、前瞻性、随机对照的临床研究, 希望能对 AIS-LVO 患者 MT 术后的 BP 管理提供参考。

5. 总结

综上所述, AIS-LVO 作为 AIS 救治的最关键类型, MT 术后 BP 控制水平对该类人群的临床转归至关重要。目前 AIS-LVO 患者 MT 术后的 BP 管理方案尚未有明确结论, 神经科医生主要在指南及专家共识的引领下, 根据患者术后血管再通状态、术后症状性颅内出血的发生风险、急性脑梗死组织范围大小和责任病变处侧枝循环建立情况及脑血流的监测情况等多种因素进行综合管理。未来可能需要更多大型的前瞻性的临床研究来探究 AIS-LVO 患者 MT 术后 BP 管理方案。

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