·专论·

高血压脑出血外科手术治疗

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【摘要】 高血压脑出血发病率、病死率和病残率均较高，相较药物保守治疗，外科手术治疗的有效性尚存争议，但外科手术是改善高血压脑出血患者预后最有前景的方法。目前手术方式主要有3种，开颅血肿清除术可以直视下清除血肿，止血可靠，但手术切口较大、手术时间较长、术中出血较多，神经功能恢复常不够理想；血肿穿刺置管引流术手术切口较小，对正常脑组织影响较小，但血肿清除不彻底，可能增加颅内感染风险；神经内镜下血肿清除术手术切口较小，可以有效减少神经纤维束损害，血肿清除彻底。上述3种手术方式的疗效尚缺乏前瞻性临床研究证实，期待微创手术和开颅手术治疗幕上高血压脑出血比较（MISICH）研究可以提供高质量的研究数据和高级别的循证医学证据。

【关键词】 颅内出血，高血压性； 神经外科手术； 综述

Surgical treatment of hypertensive intracerebral hemorrhage

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【Abstract】 Hypertensive intracerebral hemorrhage (ICH) is a disease with high morbidity, disability rate and mortality. Compared with conservative treatment, the effectiveness of surgery is still controversial. However, surgery is the most promising treatment to improve prognosis of hypertensive ICH. There are currently three main surgical methods. Craniotomy removes the hematoma under microscope and can achieve reliable hemostasis. Limited by large trauma, relatively long operation time and massive bleeding in operation, the neurological function recovery of patients treated by this procedure is not ideal. Hematoma puncture and catheter drainage brings least injury to normal brain tissue. Nevertheless, the neurosurgeon is unaware of the intracranial situation when operating, and urokinase injection may increase the risk of intracranial infection. Endoscopic hematoma evacuation can completely remove the hematoma, which is less invasive and may avoid damage to nerve fiber bundle. Prospective studies investigating the efficacies of these three surgical approaches are lacking, while the Minimally-Invasive Surgery versus Craniotomy in Patients with Supratentorial Hypertensive Intracerebral Hemorrhage (MISICH) study is expected to provide better data and evidence.

【Key words】 Intracranial hemorrhage, hypertensive; Neurosurgical procedures; Review

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脑卒中是一种起病急骤的脑组织血液循环障碍性疾病。2016年全球疾病负担研究（GBD 2016）显示，脑卒中是中国居民首位死亡原因[1]。出血性卒中约占全部脑卒中的20%，但与缺血性卒中相比，其病死率和病残率更高、危害更大，且出血性卒中引起的死因别死亡（CSD）和因早死所致的寿命损失年（YLL）均高于缺血性卒中[2]。中国一直是全球出血性卒中发病率最高的国家之一，并且呈逐年升高趋势，截至2010年，我国出血性卒中发病率高达159/10万[3]，其中约80%为高血压脑出血，仅15%患者可于发病后30天实现生活完全自理[4]，给患者家庭和社会带来巨大经济负担。高血压脑出血也是我国重大慢性非传染性疾病防控研究的重要内容。过去数十年间，因脑出血住院治疗的病例数显

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著增加，主要与老年人口比例增加、高血压发病率升高、抗血小板药和抗凝药应用增多有关[5-6]。目前高血压脑出血的治疗方法主要包括药物保守治疗和外科手术治疗，本文拟对高血压脑出血的外科手术治疗方法进行概述。

一、高血压脑出血后脑组织损害的病理生理学机制

高血压脑出血后脑组织病理生理改变大致分为两个阶段：第一阶段，因急性脑出血和早期出血性扩张，血肿中央区出现神经细胞损伤，血肿周围水肿（PHE）区出现神经细胞凋亡、坏死和炎性因子诱导的细胞浸润[7]；血肿机械性压迫破坏神经元和神经胶质细胞，引起低血糖，并诱导神经递质释放、线粒体功能障碍和神经细胞胞膜去极化[8]；神经元和神经胶质细胞损害程度取决于线粒体功能障碍严重程度，轻微者神经细胞出现短暂性代谢抑制，严重者神经细胞发生肿胀甚至坏死。第二阶段，脑组织继发级联损害，凝血块和血红蛋白分解，尤其是凝血酶激活小胶质细胞，活化的小胶质细胞释放炎性因子等产物，诱导血-脑屏障（BBB）破坏，导致血管源性脑水肿和神经细胞凋亡[9-10]。

二、高血压脑出血的外科手术理念

目前，高血压脑出血的治疗方法主要分为药物保守治疗和外科手术治疗。国际脑出血外科手术试验（STICH）及其Ⅱ期试验（STICH Ⅱ）均未证实高血压脑出血患者可以从外科手术中获益，但上述临床研究排除存在脑疝风险的患者，药物保守治疗组有>20%的患者因病情恶化交叉行外科手术治疗，使研究结果存在偏倚，限制其临床推广应用[11-13]。外科手术清除颅内血肿，可以解除血肿占位效应，改善周围脑组织缺氧缺血情况，还可以减少血肿分解吸收时产生的毒性物质，进而减少继发性脑组织损害[14]，这是高血压脑出血外科手术治疗的理论基础。有效清除颅内血肿，降低颅内压，防止脑疝形成；彻底止血，避免血肿不断扩大和压迫，从而最大限度地减少对重要脑区和神经纤维束的损害，是高血压脑出血外科手术治疗的主要技术要求。

三、高血压脑出血的主要外科手术方式

目前，高血压脑出血的外科手术方式主要包括3种，即开颅血肿清除术、血肿穿刺置管引流术（包括各种软通道和硬通道）和神经内镜下血肿清除术，其中，血肿穿刺置管引流术和神经内镜下血肿清除术是高血压脑出血的微创手术方式。高血压脑出血的最常见出血部位是基底节区，其次是皮质下和丘脑，小脑和脑干出血者相对少见；约40%的高血压脑出血患者伴发脑室出血，且是预后不良的危险因素[15-16]。出血部位是选择手术方式的重要参考依据。

1. 开颅血肿清除术　开颅血肿清除术是高血压脑出血外科手术的基石。神经外科医师于20世纪初即开始探索外科手术治疗高血压脑出血，最早由Cushing医师于1903年完成2例高血压脑出血患者的外科手术。目前，开颅血肿清除术已从传统的标准大骨瓣开颅血肿清除术联合去骨瓣减压术发展为小骨窗手术或锁孔手术。这种手术方式可以充分显露血肿，清晰辨认解剖学结构，止血可靠，并可以根据术中脑组织肿胀情况确定是否行去骨瓣减压术，但手术切口较大、时间较长、并发症相对较多，尤其对幕上出血的作用一直存有争议[17]。STICH试验纳入27个国家83个医疗中心的1033例高血压脑出血患者，随机分为早期开颅血肿清除术组（手术组）和药物保守治疗组（药物组），结果显示，手术组26.07%（122/468）患者获得良好结局，药物组23.79%（118/496）患者获得良好结局，两组病死率和功能结局差异均无统计学意义（$P>0.05$），表明早期开颅血肿清除术不能有效改善高血压脑出血患者预后；应注意的是，该项研究药物组有26.47%（140/529）患者因病情恶化交叉行外科手术治疗[11]。进一步的STICH Ⅱ试验则证实对于幕上表浅部位出血，开颅血肿清除术可以使患者生存获益[12]。由于颅后窝空间狭小，小脑出血后发生的梗阻性脑积水或占位效应压迫脑干时，病情进展迅速，采用开颅血肿清除术预后较好，尤其是对于脑池受压患者[18-19]。小骨窗手术或锁孔手术的普及使开颅血肿清除术的切口不断缩小[20]，但关于开颅血肿清除术疗效的争议依然存在。

2. 血肿穿刺置管引流术　血肿穿刺置管引流术采用各种软通道和硬通道穿刺引流血肿，根据头部CT图像准确定位穿刺点、穿刺方向和穿刺深度，到达理想穿刺靶点，抽吸或不抽吸血肿，留置引流管，术后注射重组组织型纤溶酶原激活物（rt-PA）或尿激酶持续溶解引流血肿，由于价格原因目前国内主要采用血肿腔内注射尿激酶的方法。1978年，Backlund和von Holst[21]率先报告采用立体定向血肿穿刺置管引流术治疗高血压脑出血；2016年，Hanley等[22]发表微创术与重组组织型纤溶酶原激

活物联合清除颅内出血Ⅱ期试验(MISTIE-Ⅱ)结果,证实立体定向血肿穿刺置管引流术联合rt-PA清除颅内血肿是安全的,并且可以显著减轻血肿周围水肿[23]。进一步验证其有效性的MISTIE-Ⅲ试验正在进行中。赵继宗等[24]的多中心临床研究显示,CT引导下立体定向血肿穿刺置管引流术治疗高血压脑出血的疗效优于传统开颅血肿清除术,但该项研究是非随机对照试验,其结论的证据级别较低。血肿穿刺置管引流术的关键是准确定位血肿,目前临床采用的定位方法有多种,主要包括传统CT图像结合临床经验定位、CT引导下立体定向定位、无框架神经导航定位和血肿定位贴定位等,近年来新发展出颅内血肿简易增强现实技术,通过计算机软件如3D-Slicer三维重建患者脑组织和血肿,再通过投影仪或手机APP投影准确定位血肿。不同血肿定位方法各有优缺点,准确、简易、廉价的定位方法是目前临床最需要的。血肿穿刺置管引流术操作简单,部分患者可于局部麻醉下进行,手术时间短,对脑组织损害小,不足之处是穿刺可能损伤血管而引起新的出血,术中难以止血,血肿清除不彻底,术后需多次注射尿激酶等,从而增加颅内感染风险。对于高龄或重要脏器功能障碍等不能耐受开颅血肿清除术的高血压脑出血患者,血肿穿刺置管引流术可能是一种较为理想的选择。

3. 神经内镜下血肿清除术　神经内镜下血肿清除术采取较小的骨瓣开颅,将神经内镜导引器等装置置入血肿腔以建立内镜工作通道,在神经内镜下通过吸引器抽吸和不断冲洗清除血肿。神经内镜手术要点包括内镜和相应手术器械、准确定位血肿、建立内镜工作通道和术中止血。解放军总医院最早在国际上报道通过iPhone手机软件“FUSED”和Android手机软件“Sina”实现简易增强现实技术定位幕上血肿[25-27],该定位方法简便易行,并经神经导航系统证实其具有较高的准确性。术中止血方面,除使用特制的双极电凝外,还可以使用单极电凝紧贴金属吸引器,通过金属电传导电凝止血,或使用新型具有电凝功能的吸引器。目前,神经内镜下血肿清除术主要适用于幕上出血和脑室出血,手术入路主要包括3种:额中回入路,主要适用于基底节区出血,手术路径较长,但清除血肿时导引器所需摆动的幅度较小,可最大限度地减少神经纤维束损害;顶枕叶入路,主要适用于丘脑和基底节区后部出血;就近入路,手术切口选择距离血肿最近部位,主要适用于皮质下出血[28]。神经内镜下血肿清除术的优点是,手术切口较小,对血肿周围脑组织的干扰较小,并可以减少重要神经纤维束损害;同时,还可以提供良好的照明和视野,于内镜直视下清除血肿,较为彻底,手术切口较小,时间较短,并可以减少并发症的发生,从而获得较好预后。其缺点是,手术空间较小,如果发生大出血难以控制。1989年,Auer等[29]进行的一项随机对照临床试验显示,发病后6个月,神经内镜组有40%(20/50)患者获得良好预后,而药物组仅26%(13/50)患者获得良好预后。对于脑室出血患者,与单纯脑室外引流术相比,神经内镜下血肿清除术可以显著降低远期脑积水发生率,缩短重症监护病房(ICU)住院时间,改善预后[30]。Xu等[31]进行高血压脑出血神经内镜下血肿清除术与开颅血肿清除术的对比分析,结果显示,神经内镜手术可以改善患者6个月预后。晚近一项系统评价和Meta分析显示,与药物保守治疗和颅内血肿清除术相比,神经内镜下血肿清除术可以降低幕上出血患者病死率,减少再出血风险,改善神经功能[32],但是其所纳入的文献以回顾性临床研究为主,且各项研究之间异质性较大。近年来,也有学者采用神经内镜联合显微外科手术治疗基底节区出血,其疗效是否优于单纯神经内镜下血肿清除术,尚待进一步证实[33]。

四、高血压脑出血的手术治疗时机

高血压脑出血的最佳手术治疗时机尚不确定。既往前瞻性随机对照临床试验采用的手术治疗时机范围较广泛(发病后4~96小时)[11-12, 34]。STICHⅡ试验的亚组分析显示,脑出血21小时内行外科手术治疗可以在一定程度上改善预后[12];另一项Meta分析结果显示,脑出血8小时内行外科手术治疗可以改善预后[35];但是超早期(发病4小时内)行开颅血肿清除术可能增加再出血风险[36]。研究显示,近1/3的高血压脑出血可以出现血肿扩大,绝大多数发生于发病6小时内[37],因此,高血压脑出血6小时后尽快行外科手术治疗,可能是一种较为稳妥的方案。

五、总结与展望

相较于缺血性卒中和蛛网膜下隙出血(SAH)预防与治疗研究取得的较大进展,高血压脑出血在临床研究和指南证据方面还较为落后。手术清除血肿以减轻血肿机械性压迫和继发性血管源性脑水肿是改善高血压脑出血预后最有前景的方法,目前

手术疗效不确切可能是由于高血压脑出血本身的异质性和手术损伤对不同部位的影响各异。业已证实,皮质下浅表部位出血可以从传统开颅血肿清除术中获益,这是由于破坏较少的正常脑组织即可到达血肿部位;血肿穿刺置管引流术和神经内镜下血肿清除术正好契合这一理念,以对正常脑组织损害最小的方式到达血肿部位。研究显示,以血肿穿刺置管引流术和神经内镜下血肿清除术为代表的微创手术可能优于传统开颅血肿清除术或单纯药物保守治疗[29-32];与血肿穿刺置管引流术相比,神经内镜下血肿清除术具有内镜直视下清除血肿、术中及时发现和处理出血、血肿清除率较高等优势,但神经内镜下血肿清除术具有一定的技术要求,需经过充足的技术训练。目前关于3种外科手术方式疗效比较的研究非常欠缺,且既往研究均局限于回顾性研究。一项比较开颅血肿清除术、血肿穿刺置管引流术与神经内镜下血肿清除术疗效和预后的多中心随机对照临床试验——微创手术和开颅手术治疗幕上高血压脑出血比较(MISICH)研究(试验编号:NCT02811614)[38]正在进行中,旨在总结高血压脑出血不同手术方式的最佳适应证和手术治疗时机,从而改善预后。该项研究获得"十三五"国家重点研发计划项目的资助,有望获得高质量的研究数据、提供高级别的循证医学证据,并在此基础上建立高血压脑出血个体化手术治疗体系标准。

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