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• 综述 •

## 高血压脑出血微创手术治疗进展

魏嘉良,董艳,侯立军\*

第二军医大学长征医院神经外科,上海 200003

**[摘要]** 高血压脑出血具有高发病率、高残死率,给社会、家庭带来了沉重的健康及经济负担。高血压脑出血也是脑卒中亚分类中仅有的没有明确治疗标准的疾病,传统开颅手术在高血压脑出血中应用广泛,但目前没有明确证据支持其可以提升患者的神经功能及预后;微创手术逐渐得到了越来越广泛的应用,显示出明显优势。本文主要就目前常用的高血压脑出血微创手术,包括立体定向血肿抽吸、神经内镜技术及纤溶药物治疗等的发展及现状作一综述。

**[关键词]** 高血压性颅内出血;微创性外科手术;立体定向血肿抽吸;神经内镜术;组织型纤溶酶原激活物;尿纤溶酶原激活物

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### Recent progress of minimally invasive surgery for hypertensive intracranial hemorrhage

WEI Jia-liang, DONG Yan, HOU Li-jun\*

Department of Neurosurgery, Changzheng Hospital, Second Military Medical University, Shanghai 200003, China

**[Abstract]** Hypertensive intracranial hemorrhage (HICH) has high incidence and mortality, causing great economic and health burden. However, HICH is the only subgroup of stroke that has no clear treatment standard. Though traditional craniotomy still enjoys popularity in treating HICH, yet no clear clinical evidence support its benefit to neuronal function and prognosis. Recently minimally invasive surgery (MIS) begin to show great advantage to treat HICH. This review presented the current situation and recent progress of common MIS procedures for HICH, including stereotactic aspiration, neuro-endoscopic evacuation and fibrinolysis treatment.

**[Key words]** hypertensive intracranial hemorrhage; minimally invasive surgical procedures; stereotactic aspiration; neuro-endoscopy; tissue plasminogen activator; urinary plasminogen activator

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高血压脑出血(hypertensive intracranial hemorrhage, HICH)是高血压病引起的脑内血管破裂出血性疾病,其发病率、病死率和致残率很高,虽然通过控制血压可有效降低 HICH 的发生率<sup>[1]</sup>,但 HICH 的发生率仍居高不下。根据欧洲卒中协会<sup>[2]</sup>的统计,脑出血占有所有卒中的 9%~27%,而前者中 45%以上是由高血压引起的,脑出血患者仅 46%的 1 年生存率令人堪忧,即使在 NICU 接受治疗, HICH 的死亡率也高达 28%~38%<sup>[2]</sup>。根据美国心脏协会/美国卒中协会(AHA)的统计, HICH 患者 6 个月内的神经功能恢复至可独立生活者不到 20%<sup>[3]</sup>。在中国,出血性卒中发生率由 1990 年的 84.1/万人提高到了 2014 年的 100.9/万人以上<sup>[2]</sup>,

也就是说, HICH 的发生率为(4~5)/万人。 HICH 患者为社会、家庭带来了沉重的健康及经济负担,且由于缺乏明确的医学干预标准, HICH 的治疗方法选择不可避免成为当前临床决策的难题。目前对于 HICH 的治疗,由于缺乏强有力的循证医学证据以及患者病情及来源的不均一性,无论手术治疗抑或保守治疗,均无绝对的预后改善证据<sup>[2-4]</sup>,而由于大量临床研究结果的褒贬不一, HICH 的手术指征也很难形成广泛的共识<sup>[5-8]</sup>。更为重要的是,目前界内对手术治疗 HICH 时机的选择仍有争议<sup>[9-10]</sup>。而由于临床 STICH<sup>[11]</sup> 实验及其亚组实验 STICH II<sup>[12]</sup> 结果的显著差异, HICH 患者的治疗时机及方式选择的分歧仍显而易见。

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**[作者简介]** 魏嘉良, 硕士, 住院医师. E-mail: kimi\_wei@126.com

\* 通信作者 (Corresponding author). Tel: 021-81885671, E-mail: lj\_hou@yahoo.com

国际卒中大会(ISC)在2004年提出“血肿体积减少越多,患者预后越好”的理论,提示手术治疗HICH的重要性。开颅血肿清除是长期以来神经外科治疗HICH的主流,对于颅内高压的患者,开颅血肿清除的同时也可行去骨瓣减压以降低脑疝发生的风险,很多HICH患者在接受开颅血肿清除(包括可能的去骨瓣减压)后获得了理想的治疗效果<sup>[13]</sup>。然而由于患者各项指标及疾病状况的异质性、不同的辅助治疗方式及脑出血在不同患者身上的具体情况的差别,到目前为止仍没有一个试验可以提供明确的证据以证明开颅手术可提升患者的神经功能,同时由于开颅本身对患者造成的创伤使得其对于血肿尤其是深部血肿的清除效果可能弊大于利<sup>[11]</sup>。随着手术器械及材料的快速发展,微创手术治疗HICH逐渐受到关注。从20世纪60年代以来,经过不断地实践、改进,微创手术逐渐成为治疗HICH的重要方法。经过多年的发展,微创神经外科目前主要包括立体定向神经外科、内镜神经外科、放射神经外科、血管内神经外科<sup>[14]</sup>。本文主要综述立体定向穿刺血肿抽吸术及神经内镜下血肿清除术,前者依据其不同的定位方法又分为框架立体定向及无框架式立体定向血肿抽吸术,为后续研究奠定基础。

## 1 立体定向穿刺血肿抽吸术

随着CT的问世,Backlund和VonHolst在1978年提出一种新设计的立体定向血肿排出装置,并成功实施脑内血肿清除术。随着诊断、治疗技术的快速发展,Higgins在1980年和1982年对此类技术做了改进,其后不少学者通过立体定向穿刺血肿抽吸术治疗HICH患者取得了较保守治疗更为理想的效果<sup>[15-16]</sup>。而SICHPA试验同样证实了立体定向血肿抽吸术的安全性及相对于保守治疗在清除血肿方面的优势<sup>[8]</sup>。在很长一段时间内,框架立体定向血肿抽吸术是抽吸深部血肿的金标准<sup>[17]</sup>。初期的框架立体定向血肿抽吸术由于其仅依靠轴位CT图像确定穿刺点造成穿刺点的局限性,只能评估血肿的前部和后部,使得血肿体积的清除速度差强人意<sup>[18]</sup>。其后有学者对此类术式进行了改进,利用轴位、矢状位、冠状位的影像学资料,经计算机计算出 $x$ 、 $y$ 、 $z$ 三点坐标值,安装导向装置并校对靶点坐

标。选择脑部非功能区,尽量避开脑部重要血管,通过导向仪钻孔置入穿刺针抽吸血肿并可留置引流管以进一步引流血肿,也有学者进行多中心血肿抽吸,并取得了不错的效果<sup>[19-20]</sup>。在我国,由于框架式立体定向血肿抽吸术具有步骤相对复杂、耗时长且对精准度要求高的缺点,使其应用受到一定的限制,尤其是针对急需抢救的患者。同时,由于我国医疗资源不均衡,基层医院甚至内陆西部地区部分中型医院缺乏必要的立体定向仪器,使得立体定向技术并不适于我国基层普遍应用,从而逐渐出现了较为简单的定向穿刺方法。1994年,我国学者结合颅内血肿抽吸引流与立体定向研制完成了使用YL-1型一次性颅内血肿穿刺针进行颅内血肿微创清除技术,其基本原理是以最大层面的血肿中心为穿刺靶点,靶点距离头皮最近点为穿刺点,穿刺轨迹平行于CT平扫平面,垂直于矢状线。对于单凭CT片可能较难判断穿刺点的,可以在根据初次CT结果所定的穿刺点固定标记物后再次进行CT检查以矫正穿刺点,其后使用YL-1型一次性颅内血肿穿刺针,在电钻动力驱动下直接钻颅进入血肿,快速建立起清除血肿的硬通道,采用振荡手法注入生理盐水,在血肿内融出一小洞,再应用针型血肿粉碎器粉碎部分血肿后注入液化剂液化引流冲洗,达到清除血肿的目的<sup>[21]</sup>。由于YL-1型一次性颅内血肿穿刺针是局麻下小创伤穿刺(直径约3 mm),采用硬通道技术,具有不切割神经、不需缝合即可将长期留置穿刺针等优点,在我国尤其是基层医院的应用中取得了良好的效果<sup>[22-25]</sup>。

随着影像学及神经导航技术的发展,1986年Robert及其同事介绍了一种与CT图像、显微镜相结合的无框架式定向手术系统,无框架立体定向抽吸血肿的步骤为:通过CT或MRI获取图像;患者注册(即将影像资料与手术床上患者术野准确地连接起来);确定穿刺点;钻孔;确定穿刺轨道;抽吸血肿。无框架立体定向装置的核心是神经导航装置,神经导航系统能对虚拟的数字化影像与神经系统实际解剖结构之间建立起动态关系,它具有三维空间定位和术中实时导航功能,实时向神经外科医生反馈手术过程。再加上1997年Dorward设计的相似装置在脑组织定向活检应用的良好表现<sup>[26]</sup>,使得此类系统逐渐得到了重视和发展。虽然有学者认为无

框架式定向手术系统对疾病转归的影响并未有明显改善,且在实践过程中发生导管放置异位的概率更高甚至术后感染等并发症的发生率大于内科保守治疗,但仍有不少学者<sup>[18,27-29]</sup>对其安全性及血肿清除有效性持肯定态度。

## 2 神经内镜手术

1989 年 Auer 等<sup>[30]</sup>应用神经内镜手术治疗自发性脑出血患者使得患者生存率由保守治疗的 30% 上升至 70% 且大大提高生存患者治疗预后,使得神经内镜手术被广泛应用于 HICH 患者的治疗。神经内镜技术相较于立体定向技术,血肿清除率更高、病死率更低、并发症发生更少、手术时间更短<sup>[31]</sup>。Zan 等<sup>[32]</sup>认为神经内镜的优点有:(1)神经内镜使得术者可直视血肿腔,更易找到出血点,使得术后再出血概率下降;(2)由于更广阔的视野使得血肿清除率更高;(3)对脑组织损伤及牵拉更小;(4)更短的手术时间。其后不少学者对于神经内镜辅助清除血肿都持肯定态度<sup>[8,33]</sup>。然而,神经内镜仍存在不少不足:受限的视野范围、受限的操作空间、难以控制的方向感、出血造成的视野模糊及内镜本身存在的可视盲点等<sup>[34]</sup>。

对此,在应用神经内镜技术的过程中,不断有学者对其进行改良与完善。Nishihara 等<sup>[35]</sup>为获得更好的术中内镜视野及更及时地发现活动性出血点,对神经内镜血肿清除技术进行了改进,使用透明穿刺鞘治疗了 9 例出血量平均在 88 mL 的患者,血肿清除率高达 86%~100%,且术后均有神经功能改善。Nakano 等<sup>[36]</sup>认为,有了神经内镜的辅助,CT 介导下的立体定向血肿清除更加安全可靠,而超声吸引器的应用可使得血肿清除率进一步提升。但其认为神经内镜的手术适应证为:(1)小于 40 mL 的血肿;(2)深部血肿(如丘脑出血);(3)出血破入脑室;(4)无法耐受全麻的高风险患者。Hsieh 等<sup>[37]</sup>对穿刺鞘进行了改进,使得术中视野增加且无需盐水冲洗就能获得良好的视野,内镜血肿清除率基本在 91%~97%。Bakshi 等<sup>[38]</sup>使用了内镜、冲洗、电凝三合一的新型内镜,术中不再需要鞘管而使术者有更大的可操作性;Nagasaka 等<sup>[39]</sup>使用冲、吸结合的新型内镜,反复冲洗吸除,提供更为清晰的手术视野使得止血更为安全、彻底;也有学者应用 CT 三维重

建技术以提供更精准的影像学资料使得内镜下血肿清除更加安全、有效<sup>[40]</sup>。

由于颞部入路可以最短距离到达血肿腔,使得其成为神经内镜技术的常见入路。但也有学者持不同意见:Hsieh 等<sup>[37]</sup>认为,对于前后径较长的、尤其是 >50 mL 的血肿,使用前入路而非颞侧入路可获得更好的血肿清除效果,因为前入路主要损伤的是脑哑区,同时前入路可提供更好的视野以清除前部血肿;Dye 等<sup>[41]</sup>同样认为经眉/锁孔前入路清除基底节前部血肿的效果更好。而 Chen 等<sup>[42]</sup>认为,对于出血量 ≤50 mL 者尤其是老年患者,经外侧裂入路可以更好地清除血肿且操作简单、安全且对脑功能区损伤很少,但其同时承认,由于脑部解剖学特点的限制,经外侧裂入路很难清除顶叶血肿,但由于 HICH 常见出血点并不在顶叶,故经外侧裂入路可用于治疗大部分 HICH 患者。

## 3 rt-PA/尿激酶纤溶治疗

在 HICH 的微创手术治疗过程中,单纯物理去除血肿并不能获得很好的预后效果,而理论上讲,纤溶药物既可通过减少血肿体积以减少占位效应,同时又抑制了凝血酶及其他化学性因素对于脑组织的进一步损伤。自 20 世纪 80 年代末期开始,不少学者先后在小鼠及患者体内应用纤溶药物溶解血凝块并取得了良好的效果,使得纤溶药物辅助液化血肿治疗受到越来越多的关注<sup>[43]</sup>。然而也有部分学者质疑纤溶药物辅助治疗 HICH 患者的危险性,Yepes 等<sup>[44]</sup>及 Keric 等<sup>[45]</sup>认为 rt-PA 的使用虽然减小了血肿的体积,却加重了迟发型血肿周围水肿的严重程度。而部分学者得出相反的结论<sup>[46-47]</sup>。同时,虽然不少学者经过临床试验,发现纤溶治疗并未显著提升再出血的风险,并肯定了尿激酶治疗脑出血破入脑室的可行性及安全性<sup>[17,48-49]</sup>;但 SICHPA 试验使用 5 000 U 的尿激酶+1 mL 生理盐水,导管内注入,每隔 6 h 一次,共 8 次,虽取得了较为理想的血肿清除效果,但患者再出血率高达 21.9%<sup>[8]</sup>,提示纤溶药物的使用与再出血间的关系仍有待进一步探究。目前仍没有大规模临床随机试验证实纤溶药物对于 HICH 疗的绝对效果及风险,且尚无标准的纤溶治疗方案,但 2013 年国际卒中大会 (ISC) 报告的最新研究结果表明,微创手术加 rt-PA 治疗脑出

血(MISTIE)较药物治疗更为安全,脑出血患者能从MISTIE治疗中获益,预示着纤溶药物辅助治疗HICH的乐观前景<sup>[50]</sup>。

#### 4 展望

2000年Fernandes等<sup>[51]</sup>认为传统手术治疗脑出血的不确定性让人存疑;同样的,虽然微创手术治疗HICH明显改善了患者预后,但由于缺乏确凿的临床手术证据加上当前临床试验结果的参差不齐及多样化结局的现状,使得微创手术治疗HICH仍处于试行阶段。此外,由于缺乏足够的大规模临床RCT研究,同时考虑到HICH患者巨大的异质性,虽然目前有不少正在进行的大规模研究评估各种治疗方法治疗HICH的效果,如MISTIE III及CLEAR III研究,且已有了初步积极的结果,但仍不足以盖棺定论,就目前而言,不确定性仍在继续,仍需要更多的大规模多中心随机对照研究以对微创手术治疗HICH有更准确的定位。

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