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# 自发性幕上性脑出血的诊疗现状与进展

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## 摘　要

**自发性幕上性脑出血是最致命的卒中类型之一，存活的患者面临着不良功能结局的风险。脑淀粉样血管病和深穿支动脉病是最常见的病因，其病理生理遵循一个复杂且动态的过程，即血管破裂、初始血肿形成、血肿和周围水肿扩张引起的直接机械性损伤，以及血肿及其代谢产物介导的继发性损伤。虽然局灶性神经功能缺损和非特异性症状是脑出血的主要临床表现，仍需要完善辅助检查进行鉴别。自发性幕上性脑出血属于神经科急症，尽早明确诊断、提供生命支持与接受卒中单元护理至关重要。相关治疗主要集中于止血治疗、血压控制和外科干预。此外，康复治疗和长期管理有助于改善预后，减少复发，部分新兴疗法展现出潜力。尽管缺乏特定有效的治疗方法，但外科干预尤其是微创手术可能改善患者的预后，为临床诊疗带来了新希望。**

## 关键词

**自发性幕上性脑出血，病理生理，临床表现，诊断，治疗**

# Current Status and Advances in Diagnosis and Treatment of Spontaneous Supratentorial Intracerebral Hemorrhage

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## Abstract

**Spontaneous supratentorial intracerebral hemorrhage is one of the most fatal subtypes of stroke,**

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**and patients who survive face the risk of poor functional outcome. Cerebral amyloid angiopathy and deep perforator arteriopathy are the most common etiologies, and the pathophysiology of this condition follows a complex and dynamic process involving direct mechanical injury from vessel rupture, initial hematoma formation, and expansion of the hematoma and perihematomal edema, as well as secondary injury mediated by the hematoma and its metabolites. Although focal neurological deficits and nonspecific symptoms are the main clinical manifestations of intracerebral hemorrhage, auxiliary examinations are still required for differential diagnosis. Spontaneous supratentorial intracerebral hemorrhage is a neurological emergency; early definitive diagnosis, provision of life support, and admission to a stroke unit are crucial. Related treatment primarily focuses on hemostatic therapy, blood pressure control, and surgical interventions. In addition, rehabilitation therapy and long-term management help improve prognosis and reduce recurrence, and some emerging therapies show potential. Despite the lack of a specific and effective treatment modality, surgical interventions, particularly minimally invasive surgery, may improve patient outcomes, offering new hope for clinical management.**

## Keywords

**Spontaneous Supratentorial Intracerebral Hemorrhage, Pathophysiology, Clinical Manifestations, Diagnosis, Treatment**



## 1. 背景

自发性脑出血是指非外伤情况下脑内血管破裂导致的脑实质出血，根据出血的原因，又可进一步分为原发性或继发性[1]。原发性脑出血常起源于脑淀粉样血管病或深穿支动脉病损伤的小血管自发破裂，约占所有自发性脑出血的 78%~88% [2]。继发性脑出血仅在少数患者中发生，由血管异常(如动静脉畸形和动脉瘤)、肿瘤或凝血功能障碍等引起。由于原发性脑出血是最为常见的出血形式，继发性脑出血相对少见且存在明确的原发病因，因此本综述所讨论的自发性脑出血限定于原发性脑出血。

幕上是自发性脑出血的好发部位，约占所有新发卒中的 8%~13%，具有高发病率和高死亡率的特点[3] [4]。存活的患者多数伴有躯体残疾，还面临着不同程度的认知障碍，这种认知障碍累及多个认知领域，如语言、记忆、执行功能、处理速度和视觉空间能力[5]-[7]。超过一半的幸存者伴随有神经精神症状，以冷漠和多动最为常见[8]。此外，约有 10%的患者在发病后的数年乃至数十年内仍有癫痫发作，严重影响了患者的生活质量[9]。

由于始终缺乏循证医学证据支持的有效治疗方法，保守药物治疗(Conservative Medical Treatment, CMT)目前仍是自发性幕上性脑出血的标准治疗。然而，近年来在疾病的各个方面涌现了诸多新的研究并取得了重大突破，促使临床采取更加积极主动的措施，因此，亟需新的治疗方法和对现有方法的改进应用。本文旨在就自发性幕上性脑出血病理生理、临床表现、诊断和治疗方面的现状和进展进行总结。

## 2. 病理生理

尽管使用了原发性脑出血这一定义以与存在显著病因的出血相区分，但这些出血并非真正原发性，而是由潜在血管病理损伤引起的，脑淀粉样血管病和深穿支动脉病(也称为高血压动脉病或小动脉硬化)是最常见的病因[10] [11]。

脑淀粉样血管病通过淀粉样蛋白-$\beta$逐渐积累，降低微动脉、小动脉和中等大小动脉的血管壁顺应性，其源于机体对淀粉样蛋白-$\beta$的清除能力受损，且血管中的沉积量随年龄呈指数级增加[12] [13]。这一病理改变常见于软脑膜和浅表脑叶的血管中，并导致易复发性脑叶出血[14] [15]。

深穿支动脉病是一组与高血压相关的血管疾病，主要通过小动脉硬化、脂质蛋白沉着和纤维蛋白样坏死累及易受血压影响的深穿支微动脉和小动脉，如来自基底动脉和大脑后动脉的穿支动脉[16]。这些动脉供应大脑的深层区域，如基底节和丘脑，与深部脑出血紧密联系[17]。

然而如果简单的将脑叶出血归因于脑淀粉样血管病，深部脑出血归因于深穿支动脉病，并不准确。现有的影像学证据仅支持诊断脑淀粉样血管病[18]，深穿支动脉病尚无经过验证的特异性标志物，通常依靠排除性诊断。此外，一项关于脑淀粉样血管病相关性自发性脑叶出血的尸检研究显示，42%的患者在脑淀粉样血管病外合并有其它脑小血管病，39%的患者为其它脑小血管病，仅有 16%的患者为单纯性脑淀粉样血管病[19]。因此，二者并非简单的二元对立关系，对于老年或合并高血压的患者，可能同时患有脑淀粉样血管病和深穿支动脉病。

无论起源于何种机制，自发性幕上性脑出血都遵循一个相同、复杂且动态的脑组织损伤过程，即血管破裂、初始血肿形成、血肿和周围水肿扩张引起的直接机械性损伤，以及血肿及其代谢产物介导的继发性损伤。

在血肿形成的初期，由于原发出血源的持续出血以及对周围血管的机械性破坏，血肿具有易扩张性，约有 70%的患者在症状发作后的 24 小时内发生了不同程度的血肿扩张[20] [21]。周围水肿在血肿形成后立即出现，在初期的 48 小时内快速增长，并在第 2 周末达到峰值[22]。血肿和周围水肿对脑组织的机械破坏，导致了神经元损伤或死亡[23] [24]，同时血液成分(如红细胞和蛋白酶)从破裂血管进入脑实质[25]。随后，激活的小胶质细胞与招募的血源性白细胞合成和释放炎症因子及其它免疫活性分子，共同参与了炎症反应[26] [27]。红细胞在进入脑实质后的约 24 小时开始溶解，释放出含铁血红素，并在血红素氧合酶作用下进一步分解为游离铁和胆红素[28]。游离铁作为强氧化剂诱发氧化应激，进而对周围细胞造成损伤。基质金属蛋白酶(Matrix Metalloproteinases, MMPs)和凝血酶是继发性损伤中的关键蛋白酶。MMPs 是一类依赖钙、锌离子作为辅助因子的蛋白酶家族，其中 MMPs-9 在脑出血的病理生理过程中最为重要，与血脑屏障破坏、血管通透性增加紧密相关[29]-[32]。凝血酶除了在止血中起到核心作用，还通过激活补体系统[33]、活化小胶质细胞[34]等途径间接参与到组织损伤中。

## 3. 临床表现

自发性幕上性脑出血以急性起病为特点，伴有局灶性神经功能缺损(少数为全面性神经功能缺损)，以及一种或数种非特异性症状。局灶性神经功能缺损的表现取决于出血的位置、累及范围(血肿和水肿的大小)和损伤程度，例如内囊受累常出现对侧偏瘫、对侧偏身感觉障碍和对侧同向性偏盲，因此识别神经症状和体征有利于早期定位血肿。常见的非特异性症状包括头痛、恶心、呕吐和意识障碍，颅内压增高或血肿对相关结构的直接压迫可引起对应症状。刺激疼痛敏感的结构(如三叉神经血管系统)可导致头痛[35]，刺激延髓呕吐中枢可产生恶心和呕吐[36]，意识障碍则是间脑和脑干网状激活系统的受压的结果[37]。尽管这些症状不具有特异性，但对判断患者的病情变化至关重要[38]。

## 4. 诊断

虽然骤然出现的局灶性神经功能缺损和非特异性症状提示应优先考虑诊断为脑出血，但仍需要通过影像学检查与缺血性卒中进行区分，此外还需要完善血管检查和实验室检查与其它病因和部位的脑出血相鉴别。

头颅 CT 平扫可以快速、精准地识别和定位血肿，将其与缺血性脑卒中区分开来，并评估血肿与周围水肿体积，以及是否合并如脑室出血和脑疝，是诊断脑出血的首选影像学检查[39]。脑出血在 CT 上表现为高密度区域，这种高密度主要是由于进入脑实质的血液中的血红蛋白引起的(无论其是否位于红细胞内)，且与血红蛋白的聚集程度成线性关系[40]。在疾病的初期，由于血液外渗，血红蛋白大量堆积，血肿形成部位的密度值急剧上升，而随着病程的进展，血肿及周围组织被逐渐吸收，密度值也随之下降。

头颅 CT 平扫上的某些影像特征(如血肿内密度不均或边缘不规则) [41] [42]、计算机断层扫描血管造影(Computed Tomography Angiography, CTA)动脉期出现的“点征”[43]以及 CTA 延迟期出现的“渗漏征”[44]可能有助于识别和预测脑出血后血肿扩张的风险。这些征象在一定程度上可作为补充证据，辅助临床判断患者的病情变化和预后，尤其对于病情危重导致检查受限的患者。

头颅 MRI 平扫可借助 T1、T2 加权序列判断脑出血所处的疾病阶段(详见表 1)，对于超急性期脑出血的检测灵敏度与头颅 CT 平扫相当，而在识别 12~24 小时以后脑出血方面则更准确[45]。其他的 MRI 序列，如弥散加权成像、磁敏感加权成像和梯度回波序列等，可为脑出血的诊断与病因鉴别提供更多的影像学信息，但受限于检查时间过长和对阅片水平要求较高，因此仅推荐作为识别 12~24 小时以后脑出血的影像学检查，通常不作为急诊检查手段[46]-[48]。

**Table 1.** Evolutionary stages of intracerebral hemorrhages and their appearance on MRI on T1 and T2 weighted sequences
**表 1.** 脑出血的演变阶段及其在 MRI T1 和 T2 加权序列上的表现

| Stage | Hemoglobin | T1-Weighted | T2-Weighted | Time |
|---|---|---|---|---|
| Hyperacute | Oxyhemoglobin | Dark | Bright | Hours |
| Acute | Deoxyhemoglobin | Dark | Very dark | Days |
| **Subacute** | | | | |
| Early | Methemoglobin | Bright | Dark | Days~1 week |
| Late | Methemoglobin | Bright | Bright | 1 week~1 month |
| **Chronic** | | | | >Months |
| Center | Hemachrome | Bright | Bright | |
| Rim | Hemosiderin | Dark | Very dark | |

诊断性血管造影用于诊断和鉴别与脑出血相关的血管病变[49]，常见的影像学检查包括 CTA、计算机断层扫描静脉造影(Computed Tomography Venography, CTV)、磁共振血管造影(Magnetic Resonance Angiography, MRA)、磁共振静脉造影(Magnetic Resonance Venography, MRV)和数字减影血管造影(Digital Subtraction Angiography, DSA)等。CTA 和 MRA 具有无创和快速的优点，且对颅内血管病变的检测具有高敏感性和特异性，因此常用于初步筛查可能存在的动脉血管病变[50]，相应的，对于可疑的静脉血管病变，应予以完善 CTV 和 MRV [51] [52]。DSA 可以动态显示颅内各级血管的结构和血管病变的位置、供血动脉及引流静脉，是最客观、真实和可靠的影像学诊断方法。对于部分初筛结果为阴性的患者，DSA 能够准确检测出未发现的潜在血管病变[53]。尽管对识别大血管病变极为灵敏，但脑淀粉样血管病、深穿支动脉病、血管畸形和肿瘤等往往在 DSA 上表现为阴性[54]。同时受限于其操作复杂且费用较昂贵，目前仅作为进一步确诊的选择。

此外，病史和实验室检查能为诊断病因提供更多的间接证据，例如服用抗凝抗板药物、血小板计数低下、凝血酶原时间延长或国际标准化比值升高的患者，还应考虑凝血功能障碍或药物相关性脑出血。

## 5. 治疗

### 5.1. 院前与急诊处理

早期识别对自发性幕上性脑出血的治疗和预后至关重要[55] [56]，然而在缺乏影像学检查的情况下，通常难以与其他疾病进行鉴别。因此院前与急诊的重点在于提供生命支持与尽早完善相关检查，并在诊断明确后立即启动后续治疗。

### 5.2. 卒中单元护理

与普通病房护理相比，接受卒中单元护理可有效降低患者死亡率并改善功能结局[57] [58]。其护理内容应包括但不限于持续生命体征监测、神经系统评估、血糖管理、体温管理、常见并发症(如癫痫、肺部感染和静脉血栓)的预防与管理以及对症支持治疗[59]。

### 5.3. 止血治疗

约有三分之一的患者在病程中出现了显著血肿扩张，且与早期神经功能恶化和不良预后密切相关[21] [60]。基于这一事实，止血治疗似乎能改善患者的临床转归。现有的多项研究评估了重组VIIa 因子和氨甲环酸的疗效，遗憾的是除部分特定患者人群外[61]，这些药物在限制血肿扩张方面的作用并未产生普遍获益，同时在一定程度上增加了血栓形成的风险，故而不推荐常规使用[62] [63]。

还需指出的是，止血治疗的用药时机仍不确定。多数研究选择在发病后的 3~8 小时内给予首剂药物，在更早或更晚的时间点启动治疗是否能改变干预的效果有待探索[64]-[67]。另一方面，针对表现为血肿易扩张倾向影像特征患者人群的研究中，止血治疗对最终血肿量和预后无益[68]，如何识别潜在受益人群和适应症尚不清楚。

### 5.4. 血压控制

多数患者在发病时合并急性血压升高，这是血肿及周围水肿扩张、功能结局和死亡的不利影响因素，因此，在脑出血急性期采取积极降压理应是有利的[69]-[71]。然而，两项最大规模随机对照试验的结论存在矛盾，INTERACT-2 试验显示与标准降压(收缩压 < 180 mmHg)相比，早期强化降压(收缩压 < 140 mmHg)患者的预后更佳，而 ATACH-II试验未能发现统计学意义的差异[72] [73]。

二者在设计上的差异可能有助于解释结果的不同。首先，ATACH-II试验纳入收缩压 > 180 mmHg 的患者，INTERACT-2 试验纳入收缩压 150~220 mmHg 的患者(仅有 48%的患者收缩压 > 180 mmHg)。其次，INTERACT-2 试验招募了 2839 名患者，ATACH-II试验则在招募 1000 名患者后被终止，在样本量上差距过大。另外，INTERACT-2 试验允许使用不同的降压药物进行降压，而 ATACH-II试验统一使用尼卡地平。最后，ATACH-II试验在随机分配后前 2 小时强化降压组的平均收缩压为 129 mmHg，标准降压组为 141 mmHg。INTERACT-2 试验中，强化降压组首小时平均收缩压为 150 mmHg，标准降压组为 164 mmHg。ATACH-II试验降压治疗更积极，标准降压组的早期收缩压与 INTERACT-2 试验强化降压组相近。

虽然有观点认为，脑出血患者的血压升高是未控制的慢性高血压、机体应激或对颅内压增高生理反应的结果，强化降压可能引起脑灌注压不足导致缺血性脑损伤或其他缺血并发症[74]，但 INTERACT-2 和 ATACH-II试验并未发现与严重并发症的增加相关。

此外，一项 INTERACT-2 和 ATACH-II试验的合并分析指出收缩压每降低 10 mmHg，功能恢复的概率增加 10%，直至 120~130 mmHg，而在 1 小时内降低≥60 mmHg 将增加不良预后的风险[75]。

总体而言，对于收缩压在 150~220 mmHg 的患者早期均匀降压且控制血压在 130~140 mmHg 是安全

的，尽管其有效性尚不明确。对于收缩压 > 220 mmHg 的患者，由于缺乏足够的数据，可在严密监测生命体征的情况下适当降压。

### 5.5. 外科干预

#### 5.5.1. 开颅血肿清除术

外科干预的目的是减轻占位效应，阻止血肿代谢产物的释放，以减少继发性损伤。大型随机对照试验 STICH 试验旨在比较自发性幕上性脑出血的开颅血肿清除术(Craniotomy, CR)与 CMT，结果显示早期手术的功能结局与死亡率均没有获益[76]。随后的 STICH II 试验纳入了自发性脑叶出血的患者进行研究，同样取得了阴性结果，与 CMT 没有显著差异[77]。

然而，STICH II 试验基于年龄、随机化时的 GCS 评分和血肿体积的预后预测亚组分析表明，预后预测较差的患者早期手术比初始 CMT 更有可能获得良好结局，相反，手术对预后预测良好的患者没有优势。一项单中心随机对照试验发现，对于 GCS 评分 4~8 分、血肿体积 31~60 mL、中线移位 > 5 mm、合并脑室出血且无瞳孔不对称的患者，手术可降低死亡率[78]。另一项包含 STICH II 试验在内的荟萃分析显示早期手术可能带来益处，但纳入的多数研究存在潜在发表偏差[79]。

虽然 CR 在改善患者功能结局和死亡率方面的作用有待进一步验证，基于有限的数据，对病情危重的患者，手术仍可作为必要时挽救生命的措施。

#### 5.5.2. 去骨瓣减压术

去骨瓣减压术(Decompressive Craniectomy, DC)通过去除部分颅骨，提供额外空间，从而缓解颅内压增高。回顾性研究和荟萃分析表明相较于 CMT 或 CR，DC 是安全且可行的[80] [81]。SWITCH 试验显示在深部自发性幕上脑出血患者中，DC 可能优于 CMT，但统计学效力较弱[82]。鉴于缺乏足够数量的随机对照试验证据，DC 的安全性和有效性还需进一步评估，因此仅推荐作为急救手段，根据个体情况作出手术决策。

#### 5.5.3. 微创手术

与 CR 相比，微创手术可在实现清除血肿的同时最大限度减少干预造成的损伤。早期的 SICHPA 试验表明立体定向血肿穿刺引流术(Stereotactic Aspiration, SA)联合尿激酶溶栓治疗与 CMT 相比是安全的，尽管在预后上二者并无统计学差异[83]。迄今为止最大规模的 MISTIE III 试验发现接受 SA 联合阿替普酶溶栓治疗的患者死亡率显著低于 CMT，且没有增加不良事件发生的比例，但未改变功能结局[84]，这一结论在一项对比神经内镜下颅内血肿清除术(Endoscopic Evacuation, EE)和 CMT 的研究中也得到了验证[85]。一些规模稍小的随机对照试验显示，与 CMT 相比，微创手术具有功能结局获益[86] [87]。

综合来看，微创手术在技术上是安全可靠的，可能有助于降低死亡率。对于其改善功能预后的结论，证据则略显不足。

现有的数据暂不支持解决关于手术时机、手术方式和手术适应症的问题。例如，多数 CR 的研究纳入了>10 mL 血肿的患者，而微创手术的研究普遍使用>20 mL 的血肿体积作为纳入标准。这种方法学上的差异难以单纯通过统计学的分析消除，亟待聚焦于手术先验问题的临床试验为未来的研究设计提供统一的参考依据。

## 6. 脑室出血

脑室出血是自发性幕上性脑出血的常见合并表现，发生率高达 36%~46% [88]。根据出血的来源可分为两类：原发性脑室出血和继发性脑室出血。原发性脑室出血相对罕见，仅占所有颅内出血的 3.1%，是

指血肿局限于脑室系统内，或起源于距脑室壁 15 mm 以内的出血[89]。继发性脑室出血则由距脑室壁 15 mm 以外的脑实质血肿破裂进入脑室形成。除血肿和脑室扩张引起的直接机械性损伤、血肿及其代谢产物介导的继发性损伤外，脑室出血的病理生理变化还涉及对脑脊液循环的影响[90]。约半数患者最终发展为不同程度的脑积水[91]，其主要机制分为两种：血肿引起的阻塞效应导致的急性梗阻性脑积水，以及血肿代谢产物引起的脑室邻近脑组织和蛛网膜的炎症反应导致的慢性交通性脑积水[92] [93]。

一项基于 STICH 试验的事后分析指出，脑室出血和脑积水的存在预示着不良的预后[94]。而在 INTERACT-2 试验的队列中，脑室出血体积与自发性幕上性脑出血患者的中重度残疾和早期死亡率有显著相关性[95]。另一项前瞻性研究显示，即使是 1 mL 的脑室出血，也与较差的功能结局密切相关[96]。

鉴于脑室出血与预后高度相关，外科干预被引入以减少损伤，降低脑积水发生的风险，并改善患者的临床转归。脑室外引流术是治疗脑室出血的首选方法，相较于 CMT 能显著降低死亡率[97]。然而，持续存在的脑室内积血易形成血栓堵塞，需多次更换引流管或长时间引流，致使颅内压控制不佳和感染风险增加[98]-[100]。溶栓治疗有助于减少血栓形成，减轻血肿占位效应，维持引流管通畅，多项回顾性研究和随机对照试验评估并证实了其在脑室出血中的安全性和有效性[101]-[103]。CLEAR III 试验将脑室外引流术联合阿替普酶溶栓治疗与单纯脑室外引流术进行比较，结果表明联合治疗是安全的，并能降低死亡率，但未显示在功能结局上的益处[104]。

脑脊液引流是缓解与脑室出血相关的颅内压增高的有效方法，对于无明显占位效应的轻度脑室出血患者，腰池外引流术是一种无需手术即可降低颅内压的更实用方法[105] [106]。一些探索性的小型随机对照试验发现，脑室外引流术进一步联合腰池外引流术治疗可改善引流情况，并降低后期行脑室分流术的比例[107] [108]。但由于相关研究数量较少，结果难以推广，需要大规模多中心研究，甚至随机对照试验，以更好地理解腰池外引流术在脑室出血中的潜在益处。

另一方面，神经内镜下脑室血肿清除术或许是治疗脑室出血的有效方法。一项比较神经内镜下脑室血肿清除术和脑室外引流术的回顾性研究显示，接受内镜手术的患者功能恢复更好，但在死亡率上并无显著差异[109]。此外，一项评估神经内镜下脑室血肿清除术在脑室出血中疗效与安全性的荟萃分析表明，其在改善功能结局，降低死亡率的同时，减少了对脑室分流术的依赖，但受限于数据较少，必须通过更多研究以证实[110]。

尽管对功能结局的影响尚不确定，在合并脑室出血的患者中，早期实施脑室外引流术(无论联合溶栓治疗与否)可减少脑积水的概率，降低死亡率。有关腰池外引流术和神经内镜下脑室血肿清除术的研究可能在未来提供全新观点。

## 7. 康复治疗与长期管理

轻至中度残疾的患者，早期接受康复治疗能有效降低死亡率，并增加功能独立的可能性[111]。值得注意的是，认知障碍和神经精神症状在自发性幕上性脑出血患者中普遍存在，约有 20%的患者在发病后存在抑郁[112]，33%的患者出现痴呆[6]，且发病率随着时间逐步增加，并与死亡率升高、不良功能预后相关。因此，识别和治疗这些并发症对康复治疗具有重大意义。

复发性出血是长期管理中的核心问题，其年度发生率约为 2.1%~5.9%，亦是导致死亡与残疾加重的重要危险因素[113]。PROGRESS 试验表明，严格控制血压是降低复发风险极为有效的措施[114]。影像学检查在复发风险评估中同样发挥着关键作用，多项研究显示，基于 MRI 发现的脑皮质表面铁沉积与复发性出血风险显著相关[115] [116]。

综上，对于自发性幕上性脑出血患者应尽早开展结合躯体与心理的康复治疗，长期控制血压，以及定期完善包括影像学检查在内的随访。

## 8. 新兴疗法与未来展望

针对出血发生后继发性损伤造成的神经功能持续恶化，加速内源性血肿清除，包括血肿及其代谢产物，是一种颇具前景的治疗策略。该过程主要涉及三个关键机制：1) 小胶质细胞和巨噬细胞通过多种受体介导的红细胞吞噬；2) 特异性途径的溶血产物清除；3) 脑淋巴系统和硬脑膜淋巴引流[117]。虽然存在诸多理论上的治疗靶点，但现有的研究结果暂未发现能够有效调控这一过程的核心药物。溶血产物中的游离铁参与了继发性损伤中的氧化应激，围绕这一靶点，一项研究探究了铁螯合剂右旋糖酐铁在自发性幕上性脑出血患者中的应用，结果表明该药物安全性良好，但与安慰剂相比，并未改善患者 90 天时的功能结局。不过在此时间点后患者的功能结局仍观察到持续改善的趋势，提示采用更长随访周期的临床试验可能有助于发现远期获益[118]。另一个潜在的治疗靶点是触珠蛋白，这是一种参与血红蛋白－触珠蛋白－分化簇 163 清除溶血产物过程的急性期蛋白。它能结合游离血红蛋白，抑制其分解为血红素和游离铁，从而避免产生毒性和炎症效应[119]。但触珠蛋白的神经保护作用受年龄、疾病阶段等多种因素的调节，其在复杂病理环境中的稳定性还需进一步检验[120]。

MRI 弥散张量成像序列通过探测水分子在脑组织中的弥散方向来三维重建关键神经纤维束，可精准判断脑出血后神经通路的损伤程度，从而指导手术路径规划以保护神经功能，并预测患者的功能恢复潜力[121]。最新发表的 ENRICH 试验评估了基于该影像序列的微创经脑沟神经纤维束旁手术在自发性幕上性脑出血患者中的疗效与安全性，结果显示与 CMT 相比，在脑叶出血的患者中手术组的长期功能结局更佳，同时短期死亡率和严重不良事件发生率更低[122]。这为微创手术的应用提供了证据支持，但其结论仍需谨慎解读。本试验仅在脑叶出血亚组中观察到手术的优势，对于更为常见的深部出血，手术的效果尚不清楚。再者，该手术方式高度依赖术中导航与纤维束成像技术，对设备条件和术者经验要求较高，且缺乏与不同手术技术的比较，其推广性与可及性有待验证。未来研究应进一步明确适宜人群、优化手术流程，并通过多中心、大样本试验探索其在不同出血部位中的普适性与长期疗效。

## 9. 总结

在过去的几十年中，自发性幕上性脑出血的病理生理、诊断和治疗领域取得了显著进展。然而，目前除卒中单元护理外，其余治疗手段的有效性缺乏高级别循证医学证据支持。在药物治疗方面，早期平稳降压是安全可行的，但能否转化为获益有待进一步验证。止血治疗在广泛人群中未能显示确切疗效，且存在血栓形成风险。外科干预方面，CR 相较于 CMT 没有优势。DC 由于缺乏安全性和有效性的数据，仅作为急救措施在个体化决策中应用。微创手术虽被证明能够降低死亡率，但改善功能结局的依据尚不充分。对于合并脑室出血者，脑室外引流术有助于降低死亡率，但功能结局未见明显差异，腰池外引流术和神经内镜下脑室血肿清除术可能是新的治疗方法。康复治疗与长期管理方面，早期康复治疗、识别并干预认知障碍与神经精神症状可降低死亡率、提高功能独立性。严格控制血压并定期影像随访可降低复发风险。新兴疗法方面，针对内源性血肿清除的多种策略(如靶向铁螯合剂、触珠蛋白等)展现出潜力，弥散张量成像引导的微创手术在脑叶出血中取得了良好效果，但均需更多研究以证实。

上述研究结果表明，外科干预尤其是微创手术可能改善自发性幕上性脑出血患者的预后，但在手术适应症、最佳时机和方法的选择等方面仍不明确，需开展研究以为临床实践和试验设计提供具体建议。同时，药物治疗、康复治疗、长期管理及新兴疗法的探索将为改善患者整体预后提供新的方向。

## 参考文献

[1] Raposo, N., Zanon Zotin, M.C., Seiffge, D.J., Li, Q., Goeldlin, M.B., Charidimou, A., *et al*. (2023) A Causal Classification System for Intracerebral Hemorrhage Subtypes. *Annals of Neurology*, **93**, 16-28. https://doi.org/10.1002/ana.26519

[2] Foulkes, M.A., Wolf, P.A., Price, T.R., Mohr, J.P. and Hier, D.B. (1988) The Stroke Data Bank: Design, Methods, and Baseline Characteristics. *Stroke*, **19**, 547-554. https://doi.org/10.1161/01.str.19.5.547

[3] Jolink, W.M.T., Wiegertjes, K., Rinkel, G.J.E., Algra, A., de Leeuw, F. and Klijn, C.J.M. (2020) Location-Specific Risk Factors for Intracerebral Hemorrhage: Systematic Review and Meta-Analysis. *Neurology*, **95**, e1807-e1818. https://doi.org/10.1212/wnl.0000000000010418

[4] Krishnamurthi, R.V., Feigin, V.L., Forouzanfar, M.H., Mensah, G.A., Connor, M., Bennett, D.A., *et al*. (2013) Global and Regional Burden of First-Ever Ischaemic and Haemorrhagic Stroke during 1990-2010: Findings from the Global Burden of Disease Study 2010. *The Lancet Global Health*, **1**, e259-e281. https://doi.org/10.1016/s2214-109x(13)70089-5

[5] Poon, M.T.C., Fonville, A.F. and Al-Shahi Salman, R. (2014) Long-Term Prognosis after Intracerebral Haemorrhage: Systematic Review and Meta-analysis. *Journal of Neurology, Neurosurgery & Psychiatry*, **85**, 660-667. https://doi.org/10.1136/jnnp-2013-306476

[6] Donnellan, C. and Werring, D. (2020) Cognitive Impairment before and after Intracerebral Haemorrhage: A Systematic Review. *Neurological Sciences*, **41**, 509-527. https://doi.org/10.1007/s10072-019-04150-5

[7] Moulin, S., Labreuche, J., Bombois, S., Rossi, C., Boulouis, G., Hénon, H., *et al*. (2016) Dementia Risk after Spontaneous Intracerebral Haemorrhage: A Prospective Cohort Study. *The Lancet Neurology*, **15**, 820-829. https://doi.org/10.1016/s1474-4422(16)00130-7

[8] Scopelliti, G., Casolla, B., Boulouis, G., Kuchcinski, G., Moulin, S., Leys, D., *et al*. (2022) Long-Term Neuropsychiatric Symptoms in Spontaneous Intracerebral Haemorrhage Survivors. *Journal of Neurology, Neurosurgery & Psychiatry*, **93**, 232-237. https://doi.org/10.1136/jnnp-2021-327557

[9] Haapaniemi, E., Strbian, D., Rossi, C., Putaala, J., Sipi, T., Mustanoja, S., *et al*. (2014) The CAVE Score for Predicting Late Seizures after Intracerebral Hemorrhage. *Stroke*, **45**, 1971-1976. https://doi.org/10.1161/strokeaha.114.004686

[10] Vinters, H.V. (1987) Cerebral Amyloid Angiopathy. A Critical Review. *Stroke*, **18**, 311-324. https://doi.org/10.1161/01.str.18.2.311

[11] Wilson, D., Charidimou, A. and Werring, D.J. (2014) Advances in Understanding Spontaneous Intracerebral Hemorrhage: Insights from Neuroimaging. *Expert Review of Neurotherapeutics*, **14**, 661-678. https://doi.org/10.1586/14737175.2014.918506

[12] Attems, J., Jellinger, K., Thal, D.R. and Van Nostrand, W. (2011) Review: Sporadic Cerebral Amyloid Angiopathy. *Neuropathology and Applied Neurobiology*, **37**, 75-93. https://doi.org/10.1111/j.1365-2990.2010.01137.x

[13] Greenberg, S.M. and Vonsattel, J.G. (1997) Diagnosis of Cerebral Amyloid Angiopathy. Sensitivity and Specificity of Cortical Biopsy. *Stroke*, **28**, 1418-1422. https://doi.org/10.1161/01.str.28.7.1418

[14] Vinters, H.V. and Gilbert, J.J. (1983) Cerebral Amyloid Angiopathy: Incidence and Complications in the Aging Brain. II. the Distribution of Amyloid Vascular Changes. *Stroke*, **14**, 924-928. https://doi.org/10.1161/01.str.14.6.924

[15] Smith, E.E. and Eichler, F. (2006) Cerebral Amyloid Angiopathy and Lobar Intracerebral Hemorrhage. *Archives of Neurology*, **63**, 148-151. https://doi.org/10.1001/archneur.63.1.148

[16] Pantoni, L. (2010) Cerebral Small Vessel Disease: From Pathogenesis and Clinical Characteristics to Therapeutic Challenges. *The Lancet Neurology*, **9**, 689-701. https://doi.org/10.1016/s1474-4422(10)70104-6

[17] Provencio, J.J., Ferreira Da Silva, I.R. and Manno, E.M. (2013) Intracerebral Hemorrhage: New Challenges and Steps Forward. *Neurosurgery Clinics of North America*, **24**, 349-359. https://doi.org/10.1016/j.nec.2013.03.002

[18] Linn, J., Halpin, A., Demaerel, P., Ruhland, J., Giese, A.D., Dichgans, M., *et al*. (2010) Prevalence of Superficial Siderosis in Patients with Cerebral Amyloid Angiopathy. *Neurology*, **74**, 1346-1350. https://doi.org/10.1212/wnl.0b013e3181dad605

[19] Rodrigues, M.A., Samarasekera, N., Lerpiniere, C., Humphreys, C., McCarron, M.O., White, P.M., *et al*. (2018) The Edinburgh CT and Genetic Diagnostic Criteria for Lobar Intracerebral Haemorrhage Associated with Cerebral Amyloid Angiopathy: Model Development and Diagnostic Test Accuracy Study. *The Lancet Neurology*, **17**, 232-240. https://doi.org/10.1016/s1474-4422(18)30006-1

[20] Kazui, S., Minematsu, K., Yamamoto, H., Sawada, T. and Yamaguchi, T. (1997) Predisposing Factors to Enlargement of Spontaneous Intracerebral Hematoma. *Stroke*, **28**, 2370-2375. https://doi.org/10.1161/01.str.28.12.2370

[21] Davis, S.M., Broderick, J., Hennerici, M., Brun, N.C., Diringer, M.N., Mayer, S.A., *et al*. (2006) Hematoma Growth Is a Determinant of Mortality and Poor Outcome after Intracerebral Hemorrhage. *Neurology*, **66**, 1175-1181. https://doi.org/10.1212/01.wnl.0000208408.98482.99

[22] Venkatasubramanian, C., Mlynash, M., Finley-Caulfield, A., Eyngorn, I., Kalimuthu, R., Snider, R.W., *et al*. (2011) Natural History of Perihematomal Edema after Intracerebral Hemorrhage Measured by Serial Magnetic Resonance Imaging. *Stroke*, **42**, 73-80. https://doi.org/10.1161/strokeaha.110.590646

[23] Qureshi, A.I., Ling, G.S.F., Khan, J., Suri, M.F.K., Miskolczi, L., Guterman, L.R., *et al*. (2001) Quantitative Analysis of Injured, Necrotic, and Apoptotic Cells in a New Experimental Model of Intracerebral Hemorrhage. *Critical Care Medicine*, **29**, 152-157. https://doi.org/10.1097/00003246-200101000-00030

[24] Qureshi, A.I., Suri, M.F.K., Ostrow, P.T., Kim, S.H., Ali, Z., Shatla, A.A., *et al*. (2003) Apoptosis as a Form of Cell Death in Intracerebral Hemorrhage. *Neurosurgery*, **52**, 1041-1048. https://doi.org/10.1227/01.neu.0000057694.96978.bc

[25] Gong, C., Hoff, J.T. and Keep, R.F. (2000) Acute Inflammatory Reaction Following Experimental Intracerebral Hemorrhage in Rat. *Brain Research*, **871**, 57-65. https://doi.org/10.1016/s0006-8993(00)02427-6

[26] Aronowski, J. and Zhao, X. (2011) Molecular Pathophysiology of Cerebral Hemorrhage: Secondary Brain Injury. *Stroke*, **42**, 1781-1786. https://doi.org/10.1161/strokeaha.110.596718

[27] Wang, J. and Doré, S. (2007) Inflammation after Intracerebral Hemorrhage. *Journal of Cerebral Blood Flow & Metabolism*, **27**, 894-908. https://doi.org/10.1038/sj.jcbfm.9600403

[28] Wagner, K.R., Sharp, F.R., Ardizzone, T.D., Lu, A. and Clark, J.F. (2003) Heme and Iron Metabolism: Role in Cerebral Hemorrhage. *Journal of Cerebral Blood Flow & Metabolism*, **23**, 629-652. https://doi.org/10.1097/01.wcb.0000073905.87928.6d

[29] Abilleira, S., Montaner, J., Molina, C.A., Monasterio, J., Castillo, J. and Alvarez-Sabín, J. (2003) Matrix Metalloproteinase—9 Concentration after Spontaneous Intracerebral Hemorrhage. *Journal of Neurosurgery*, **99**, 65-70. https://doi.org/10.3171/jns.2003.99.1.0065

[30] Castellazzi, M., Tamborino, C., De Santis, G., Garofano, F., Lupato, A., Ramponi, V., *et al*. (2010) Timing of Serum Active MMP-9 and MMP-2 Levels in Acute and Subacute Phases after Spontaneous Intracerebral Hemorrhage. *Acta Neurochirurgica Supplementum*, **106**, 137-140. https://doi.org/10.1007/978-3-211-98811-4_24

[31] Alvarez-Sabín, J., Delgado, P., Abilleira, S., Molina, C.A., Arenillas, J., Ribó, M., *et al*. (2004) Temporal Profile of Matrix Metalloproteinases and Their Inhibitors after Spontaneous Intracerebral Hemorrhage: Relationship to Clinical and Radiological Outcome. *Stroke*, **35**, 1316-1322. https://doi.org/10.1161/01.str.0000126827.69286.90

[32] Rosell, A., Ortega-Aznar, A., Alvarez-Sabín, J., Fernández-Cadenas, I., Ribó, M., Molina, C.A., *et al*. (2006) Increased Brain Expression of Matrix Metalloproteinase-9 after Ischemic and Hemorrhagic Human Stroke. *Stroke*, **37**, 1399-1406. https://doi.org/10.1161/01.str.0000223001.06264.af

[33] Amara, U., Flierl, M.A., Rittirsch, D., Klos, A., Chen, H., Acker, B., *et al*. (2010) Molecular Intercommunication between the Complement and Coagulation Systems. *The Journal of Immunology*, **185**, 5628-5636. https://doi.org/10.4049/jimmunol.0903678

[34] Möller, T., Hanisch, U. and Ransom, B.R. (2000) Thrombin-induced Activation of Cultured Rodent Microglia. *Journal of Neurochemistry*, **75**, 1539-1547. https://doi.org/10.1046/j.1471-4159.2000.0751539.x

[35] Melo, T.P., Pinto, A.N. and Ferro, J.M. (1996) Headache in Intracerebral Hematomas. *Neurology*, **47**, 494-500. https://doi.org/10.1212/wnl.47.2.494

[36] Hornby, P.J. (2001) Central Neurocircuitry Associated with Emesis. *The American Journal of Medicine*, **111**, 106-112. https://doi.org/10.1016/s0002-9343(01)00849-x

[37] Jang, S.H. and Kwon, Y.H. (2020) The Relationship between Consciousness and the Ascending Reticular Activating System in Patients with Traumatic Brain Injury. *BMC Neurology*, **20**, Article No. 375. https://doi.org/10.1186/s12883-020-01942-7

[38] Brott, T., Broderick, J., Kothari, R., Barsan, W., Tomsick, T., Sauerbeck, L., *et al*. (1997) Early Hemorrhage Growth in Patients with Intracerebral Hemorrhage. *Stroke*, **28**, 1-5. https://doi.org/10.1161/01.str.28.1.1

[39] Scott, W.R., New, P.F.J., Davis, K.R. and Schnur, J.A. (1974) Computerized Axial Tomography of Intracerebral and Intraventricular Hemorrhage. *Radiology*, **112**, 73-80. https://doi.org/10.1148/112.1.73

[40] Parizel, P., Makkat, S., Van Miert, E., Van Goethem, J., van den Hauwe, L. and De Schepper, A. (2001) Intracranial Hemorrhage: Principles of CT and MRI Interpretation. *European Radiology*, **11**, 1770-1783. https://doi.org/10.1007/s003300000800

[41] Morotti, A., Boulouis, G., Dowlatshahi, D., Li, Q., Barras, C.D., Delcourt, C., *et al*. (2019) Standards for Detecting, Interpreting, and Reporting Noncontrast Computed Tomographic Markers of Intracerebral Hemorrhage Expansion. *Annals of Neurology*, **86**, 480-492. https://doi.org/10.1002/ana.25563

[42] Morotti, A., Arba, F., Boulouis, G. and Charidimou, A. (2020) Noncontrast CT Markers of Intracerebral Hemorrhage Expansion and Poor Outcome: A Meta-Analysis. *Neurology*, **95**, 632-643. https://doi.org/10.1212/wnl.0000000000010660

[43] Wada, R., Aviv, R.I., Fox, A.J., Sahlas, D.J., Gladstone, D.J., Tomlinson, G., *et al*. (2007) CT Angiography "Spot Sign" Predicts Hematoma Expansion in Acute Intracerebral Hemorrhage. *Stroke*, **38**, 1257-1262. https://doi.org/10.1161/01.str.0000259633.59404.f3

[44] Orito, K., Hirohata, M., Nakamura, Y., Takeshige, N., Aoki, T., Hattori, G., *et al*. (2016) Leakage Sign for Primary Intracerebral Hemorrhage: A Novel Predictor of Hematoma Growth. *Stroke*, **47**, 958-963. https://doi.org/10.1161/strokeaha.115.011578

[45] Kidwell, C.S. (2004) Comparison of MRI and CT for Detection of Acute Intracerebral Hemorrhage. *JAMA*, **292**, 1823-1830. https://doi.org/10.1001/jama.292.15.1823

[46] Bradley, W.G. (1993) MR Appearance of Hemorrhage in the Brain. *Radiology*, **189**, 15-26. https://doi.org/10.1148/radiology.189.1.8372185

[47] Patel, M.R., Edelman, R.R. and Warach, S. (1996) Detection of Hyperacute Primary Intraparenchymal Hemorrhage by Magnetic Resonance Imaging. *Stroke*, **27**, 2321-2324. https://doi.org/10.1161/01.str.27.12.2321

[48] Roob, G. and Fazekas, F. (2000) Magnetic Resonance Imaging of Cerebral Microbleeds. *Current Opinion in Neurology*, **13**, 69-73. https://doi.org/10.1097/00019052-200002000-00013

[49] Zhu, X.L., Chan, M.S.Y. and Poon, W.S. (1997) Spontaneous Intracranial Hemorrhage: Which Patients Need Diagnostic Cerebral Angiography? A Prospective Study of 206 Cases and Review of the Literature. *Stroke*, **28**, 1406-1409. https://doi.org/10.1161/01.str.28.7.1406

[50] Josephson, C.B., White, P.M., Krishan, A. and Al-Shahi Salman, R. (2014) Computed Tomography Angiography or Magnetic Resonance Angiography for Detection of Intracranial Vascular Malformations in Patients with Intracerebral Haemorrhage. *Cochrane Database of Systematic Reviews*, No. 9, CD009372. https://doi.org/10.1002/14651858.cd009372.pub2

[51] Farb, R.I., Scott, J.N., Willinsky, R.A., Montanera, W.J., Wright, G.A. and terBrugge, K.G. (2003) Intracranial Venous System: Gadolinium-Enhanced Three-Dimensional MR Venography with Auto-Triggered Elliptic Centric-Ordered Sequence—Initial Experience. *Radiology*, **226**, 203-209. https://doi.org/10.1148/radiol.2261020670

[52] Wetzel, S.G., Kirsch, E., Stock, K.W., *et al*. (1999) Cerebral Veins: Comparative Study of CT Venography with Intraarterial Digital Subtraction Angiography. *American Journal of Neuroradiology*, **20**, 249-255.

[53] van Asch, C.J.J., Velthuis, B.K., Rinkel, G.J.E., Algra, A., de Kort, G.A.P., Witkamp, T.D., *et al*. (2015) Diagnostic Yield and Accuracy of CT Angiography, MR Angiography, and Digital Subtraction Angiography for Detection of Macrovascular Causes of Intracerebral Haemorrhage: Prospective, Multicentre Cohort Study. *BMJ*, **351**, h5762. https://doi.org/10.1136/bmj.h5762

[54] Lummel, N., Lutz, J., Brückmann, H. and Linn, J. (2012) The Value of Magnetic Resonance Imaging for the Detection of the Bleeding Source in Non-Traumatic Intracerebral Haemorrhages: A Comparison with Conventional Digital Subtraction Angiography. *Neuroradiology*, **54**, 673-680. https://doi.org/10.1007/s00234-011-0953-0

[55] Maas, M.B., Berman, M.D., Guth, J.C., Liotta, E.M., Prabhakaran, S. and Naidech, A.M. (2015) Neurochecks as a Biomarker of the Temporal Profile and Clinical Impact of Neurologic Changes after Intracerebral Hemorrhage. *Journal of Stroke and Cerebrovascular Diseases*, **24**, 2026-2031. https://doi.org/10.1016/j.jstrokecerebrovasdis.2015.04.045

[56] Colton, K., Richards, C.T., Pruitt, P.B., Mendelson, S.J., Holl, J.L., Naidech, A.M., *et al*. (2020) Early Stroke Recognition and Time-Based Emergency Care Performance Metrics for Intracerebral Hemorrhage. *Journal of Stroke and Cerebrovascular Diseases*, **29**, Article ID: 104552. https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.104552

[57] Langhorne, P., Fearon, P., Ronning, O.M., Kaste, M., Palomaki, H., Vemmos, K., *et al*. (2013) Stroke Unit Care Benefits Patients with Intracerebral Hemorrhage: Systematic Review and Meta-Analysis. *Stroke*, **44**, 3044-3049. https://doi.org/10.1161/strokeaha.113.001564

[58] Langhorne, P. and Ramachandra, S. (2020) Organised Inpatient (Stroke Unit) Care for Stroke: Network Meta-Analysis. *Cochrane Database of Systematic Reviews*, **4**, CD000197. https://doi.org/10.1002/14651858.cd000197.pub4

[59] Greenberg, S.M., Ziai, W.C., Cordonnier, C., Dowlatshahi, D., Francis, B., Goldstein, J.N., *et al*. (2022) 2022 Guideline for the Management of Patients with Spontaneous Intracerebral Hemorrhage: A Guideline from the American Heart Association/American Stroke Association. *Stroke*, **53**, e282-e361. https://doi.org/10.1161/str.0000000000000407

[60] Al-Shahi Salman, R., Frantzias, J., Lee, R.J., Lyden, P.D., Battey, T.W.K., Ayres, A.M., *et al*. (2018) Absolute Risk and Predictors of the Growth of Acute Spontaneous Intracerebral Haemorrhage: A Systematic Review and Meta-Analysis of Individual Patient Data. *The Lancet Neurology*, **17**, 885-894. https://doi.org/10.1016/s1474-4422(18)30253-9

[61] Mayer, S.A., Davis, S.M., Skolnick, B.E., Brun, N.C., Begtrup, K., Broderick, J.P., *et al*. (2009) Can a Subset of Intracerebral Hemorrhage Patients Benefit from Hemostatic Therapy with Recombinant Activated Factor VII? *Stroke*, **40**, 833-840. https://doi.org/10.1161/strokeaha.108.524470

[62] Al-Shahi Salman, R., Law, Z.K., Bath, P.M., Steiner, T. and Sprigg, N. (2018) Haemostatic Therapies for Acute Spontaneous Intracerebral Haemorrhage. *Cochrane Database of Systematic Reviews*, **4**, CD005951. https://doi.org/10.1002/14651858.cd005951.pub4

[63] Nie, X., Liu, J., Liu, D., Zhou, Q., Duan, W., Pu, Y., *et al*. (2021) Haemostatic Therapy in Spontaneous Intracerebral Haemorrhage Patients with High-Risk of Haematoma Expansion by CT Marker: A Systematic Review and Meta-

Analysis of Randomised Trials. *Stroke and Vascular Neurology*, **6**, 170-179. https://doi.org/10.1136/svn-2021-000941

[64] Sprigg, N., Flaherty, K., Appleton, J.P., Salman, R.A., Bereczki, D., Beridze, M., *et al*. (2018) Tranexamic Acid for Hyperacute Primary Intracerebral Haemorrhage (TICH-2): An International Randomised, Placebo-Controlled, Phase 3 Superiority Trial. *The Lancet*, **391**, 2107-2115. https://doi.org/10.1016/s0140-6736(18)31033-x

[65] Mayer, S.A., Brun, N.C., Begtrup, K., Broderick, J., Davis, S., Diringer, M.N., *et al*. (2008) Efficacy and Safety of Recombinant Activated Factor VII for Acute Intracerebral Hemorrhage. *New England Journal of Medicine*, **358**, 2127-2137. https://doi.org/10.1056/nejmoa0707534

[66] Li, X., Wang, Y.Q. and Li, W. (2012) Intervention Study on Recombinant Activated Factor VIIa in Depressing Early Hematoma Extensions of Cerebral Hemorrhage. *Chinese Journal of New Drugs*, **21**, 161-163, 216.

[67] Arumugam, A., Na, A.R., Theophilus, S.C., *et al*. (2015) Tranexamic Acid as Antifibrinolytic Agent in Non Traumatic Intracerebral Hemorrhages. *Malaysian Journal of Medical Sciences*, **22**, 62-71.

[68] Gladstone, D.J., Aviv, R.I., Demchuk, A.M., Hill, M.D., Thorpe, K.E., Khoury, J.C., *et al*. (2019) Effect of Recombinant Activated Coagulation Factor VII on Hemorrhage Expansion among Patients with Spot Sign-Positive Acute Intracerebral Hemorrhage: The SPOTLIGHT and STOP-IT Randomized Clinical Trials. *JAMA Neurology*, **76**, 1493-1501. https://doi.org/10.1001/jamaneurol.2019.2636

[69] Fogelholm, R., Avikainen, S. and Murros, K. (1997) Prognostic Value and Determinants of First-Day Mean Arterial Pressure in Spontaneous Supratentorial Intracerebral Hemorrhage. *Stroke*, **28**, 1396-1400. https://doi.org/10.1161/01.str.28.7.1396

[70] Vemmos, K.N., Tsivgoulis, G., Spengos, K., Zakopoulos, N., Synetos, A., Kotsis, V., *et al*. (2003) Association between 24-H Blood Pressure Monitoring Variables and Brain Oedema in Patients with Hyperacute Stroke. *Journal of Hypertension*, **21**, 2167-2173. https://doi.org/10.1097/00004872-200311000-00027

[71] Ohwaki, K., Yano, E., Nagashima, H., Hirata, M., Nakagomi, T. and Tamura, A. (2004) Blood Pressure Management in Acute Intracerebral Hemorrhage: Relationship between Elevated Blood Pressure and Hematoma Enlargement. *Stroke*, **35**, 1364-1367. https://doi.org/10.1161/01.str.0000128795.38283.4b

[72] Anderson, C.S., Heeley, E., Huang, Y., Wang, J., Stapf, C., Delcourt, C., *et al*. (2013) Rapid Blood-Pressure Lowering in Patients with Acute Intracerebral Hemorrhage. *New England Journal of Medicine*, **368**, 2355-2365. https://doi.org/10.1056/nejmoa1214609

[73] Qureshi, A.I., Palesch, Y.Y., Barsan, W.G., Hanley, D.F., Hsu, C.Y., Martin, R.L., *et al*. (2016) Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage. *New England Journal of Medicine*, **375**, 1033-1043. https://doi.org/10.1056/nejmoa1603460

[74] Qureshi, A.I., Bliwise, D.L., Bliwise, N.G., Akbar, M.S., Uzen, G. and Frankel, M.R. (1999) Rate of 24-Hour Blood Pressure Decline and Mortality after Spontaneous Intracerebral Hemorrhage: A Retrospective Analysis with a Random Effects Regression Model. *Critical Care Medicine*, **27**, 480-485. https://doi.org/10.1097/00003246-199903000-00021

[75] Moullaali, T.J., Wang, X., Martin, R.H., Shipes, V.B., Robinson, T.G., Chalmers, J., *et al*. (2019) Blood Pressure Control and Clinical Outcomes in Acute Intracerebral Haemorrhage: A Preplanned Pooled Analysis of Individual Participant Data. *The Lancet Neurology*, **18**, 857-864. https://doi.org/10.1016/s1474-4422(19)30196-6

[76] Mendelow, A., Gregson, B., Fernandes, H., Murray, G., Teasdale, G., Hope, D., *et al*. (2005) Early Surgery versus Initial Conservative Treatment in Patients with Spontaneous Supratentorial Intracerebral Haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): A Randomised Trial. *The Lancet*, **365**, 387-397. https://doi.org/10.1016/s0140-6736(05)70233-6

[77] Mendelow, A.D., Gregson, B.A., Rowan, E.N., Murray, G.D., Gholkar, A. and Mitchell, P.M. (2013) Early Surgery versus Initial Conservative Treatment in Patients with Spontaneous Supratentorial Lobar Intracerebral Haematomas (STICH II): A Randomised Trial. *The Lancet*, **382**, 397-408. https://doi.org/10.1016/s0140-6736(13)60986-1

[78] Bhaskar, M., Kumar, R., Ojha, B., Singh, S., Verma, N., Verma, R., *et al*. (2017) A Randomized Controlled Study of Operative versus Nonoperative Treatment for Large Spontaneous Supratentorial Intracerebral Hemorrhage. *Neurology India*, **65**, 752-758. https://doi.org/10.4103/neuroindia.ni_151_16

[79] Sondag, L., Schreuder, F.H.B.M., Boogaarts, H.D., Rovers, M.M., Vandertop, W.P., Dammers, R., *et al*. (2020) Neurosurgical Intervention for Supratentorial Intracerebral Hemorrhage. *Annals of Neurology*, **88**, 239-250. https://doi.org/10.1002/ana.25732

[80] Rasras, S., Safari, H., Zeinali, M. and Jahangiri, M. (2018) Decompressive Hemicraniectomy without Clot Evacuation in Supratentorial Deep-Seated Intracerebral Hemorrhage. *Clinical Neurology and Neurosurgery*, **174**, 1-6. https://doi.org/10.1016/j.clineuro.2018.08.017

[81] Pedro, K.M., Chua, A.E. and Lapitan, M.C.M. (2020) Decompressive Hemicraniectomy without Clot Evacuation in Spontaneous Intracranial Hemorrhage: A Systematic Review. *Clinical Neurology and Neurosurgery*, **192**, Article ID: 105730. https://doi.org/10.1016/j.clineuro.2020.105730

[82] Beck, J., Fung, C., Strbian, D., Bütikofer, L., Z'Graggen, W.J., Lang, M.F., *et al*. (2024) Decompressive Craniectomy Plus Best Medical Treatment versus Best Medical Treatment Alone for Spontaneous Severe Deep Supratentorial Intracerebral Haemorrhage: A Randomised Controlled Clinical Trial. *The Lancet*, **403**, 2395-2404. https://doi.org/10.1016/s0140-6736(24)00702-5

[83] Teernstra, O.P.M., Evers, S.M.A.A., Lodder, J., Leffers, P., Franke, C.L. and Blaauw, G. (2003) Stereotactic Treatment of Intracerebral Hematoma by Means of a Plasminogen Activator: A Multicenter Randomized Controlled Trial (SICHPA). *Stroke*, **34**, 968-974. https://doi.org/10.1161/01.str.0000063367.52044.40

[84] Hanley, D.F., Thompson, R.E., Rosenblum, M., Yenokyan, G., Lane, K., McBee, N., *et al*. (2019) Efficacy and Safety of Minimally Invasive Surgery with Thrombolysis in Intracerebral Haemorrhage Evacuation (MISTIE III): A Randomised, Controlled, Open-Label, Blinded Endpoint Phase 3 Trial. *The Lancet*, **393**, 1021-1032. https://doi.org/10.1016/s0140-6736(19)30195-3

[85] Miller, C.M., Vespa, P., Saver, J.L., Kidwell, C.S., Carmichael, S.T., Alger, J., *et al*. (2008) Image-Guided Endoscopic Evacuation of Spontaneous Intracerebral Hemorrhage. *Surgical Neurology*, **69**, 441-446. https://doi.org/10.1016/j.surneu.2007.12.016

[86] Kim, Y.Z. and Kim, K.H. (2009) Even in Patients with a Small Hemorrhagic Volume, Stereotactic-Guided Evacuation of Spontaneous Intracerebral Hemorrhage Improves Functional Outcome. *Journal of Korean Neurosurgical Society*, **46**, 109-115. https://doi.org/10.3340/jkns.2009.46.2.109

[87] Wang, W., Jiang, B., Liu, g., Li, D., Lu, C., Zhao, Y., *et al*. (2009) Minimally Invasive Craniopuncture Therapy vs. Conservative Treatment for Spontaneous Intracerebral Hemorrhage: Results from a Randomized Clinical Trial in China. *International Journal of Stroke*, **4**, 11-16. https://doi.org/10.1111/j.1747-4949.2009.00239.x

[88] Gaberel, T., Magheru, C. and Emery, E. (2012) Management of Non-Traumatic Intraventricular Hemorrhage. *Neurosurgical Review*, **35**, 485-495. https://doi.org/10.1007/s10143-012-0399-9

[89] Angelopoulos, M., Gupta, S.R. and Kia, B.A. (1995) Primary Intraventricular Hemorrhage in Adults: Clinical Features, Risk Factors, and Outcome. *Surgical Neurology*, **44**, 433-437. https://doi.org/10.1016/0090-3019(95)00261-8

[90] Wang, H., Chen, X., You, C., Wu, K. and Sun, T. (2025) Navigating Challenges in Hydrocephalus Following Intraventricular Hemorrhage: A Comprehensive Review of Current Evidence. *Frontiers in Neurology*, **16**, Article 1630286. https://doi.org/10.3389/fneur.2025.1630286

[91] Diringer, M.N., Edwards, D.F. and Zazulia, A.R. (1998) Hydrocephalus: A Previously Unrecognized Predictor of Poor Outcome from Supratentorial Intracerebral Hemorrhage. *Stroke*, **29**, 1352-1357. https://doi.org/10.1161/01.str.29.7.1352

[92] Xi, G., Keep, R.F. and Hoff, J.T. (2006) Mechanisms of Brain Injury after Intracerebral Haemorrhage. *The Lancet Neurology*, **5**, 53-63. https://doi.org/10.1016/s1474-4422(05)70283-0

[93] Mayfrank, L., Kissler, J., Raoofi, R., Delsing, P., Weis, J., Küker, W., *et al*. (1997) Ventricular Dilatation in Experimental Intraventricular Hemorrhage in Pigs. Characterization of Cerebrospinal Fluid Dynamics and the Effects of Fibrinolytic Treatment. *Stroke*, **28**, 141-148. https://doi.org/10.1161/01.str.28.1.141

[94] Bhattathiri, P.S., Gregson, B., Prasad, K.S.M. and Mendelow, A.D. (2006) Intraventricular Hemorrhage and Hydrocephalus after Spontaneous Intracerebral Hemorrhage: Results from the STICH Trial. In: Hoff, J.T., Keep, R.F., Xi, G. and Hua, Y., Eds., *Brain Edema XIII*, Springer-Verlag, 65-68. https://doi.org/10.1007/3-211-30714-1_16

[95] Chan, E., Anderson, C.S., Wang, X., Arima, H., Saxena, A., Moullaali, T.J., *et al*. (2015) Significance of Intraventricular Hemorrhage in Acute Intracerebral Hemorrhage. *Stroke*, **46**, 653-658. https://doi.org/10.1161/strokeaha.114.008470

[96] Yogendrakumar, V., Ramsay, T., Fergusson, D., Demchuk, A.M., Aviv, R.I., Rodriguez-Luna, D., *et al*. (2019) New and Expanding Ventricular Hemorrhage Predicts Poor Outcome in Acute Intracerebral Hemorrhage. *Neurology*, **93**, e879-e888. https://doi.org/10.1212/wnl.0000000000008007

[97] Nieuwkamp, D.J., de Gans, K., Rinkel, G.J.E. and Algra, A. (2000) Treatment and Outcome of Severe Intraventricular Extension in Patients with Subarachnoid or Intracerebral Hemorrhage: A Systematic Review of the Literature. *Journal of Neurology*, **247**, 117-121. https://doi.org/10.1007/pl00007792

[98] Sarmast, A., Kirmani, A. and Bhat, A. (2015) Role of External Ventricular Drainage in the Management of Intraventricular Hemorrhage; Its Complications and Management. *Surgical Neurology International*, **6**, Article 188. https://doi.org/10.4103/2152-7806.172533

[99] Aucoin, P.J., Kotilainen, H.R., Gantz, N.M., Davidson, R., Kellogg, P. and Stone, B. (1986) Intracranial Pressure Monitors. Epidemiologic Study of Risk Factors and Infections. *The American Journal of Medicine*, **80**, 369-376. https://doi.org/10.1016/0002-9343(86)90708-4

[100] Peter, S., Roman, B. and Marjan, Z. (2016) External Ventricular Drainage Infections: A Single-Centre Experience on 100 Cases. *Journal of Neurology & Neurophysiology*, **7**, 1-6.

[101] Naff, N.J., Carhuapoma, J.R., Williams, M.A., Bhardwaj, A., Ulatowski, J.A., Bederson, J., *et al*. (2000) Treatment of Intraventricular Hemorrhage with Urokinase. *Stroke*, **31**, 841-847. https://doi.org/10.1161/01.str.31.4.841

[102] Naff, N., Williams, M.A., Keyl, P.M., Tuhrim, S., Bullock, M.R., Mayer, S.A., *et al*. (2011) Low-Dose Recombinant Tissue-Type Plasminogen Activator Enhances Clot Resolution in Brain Hemorrhage: The Intraventricular Hemorrhage Thrombolysis Trial. *Stroke*, **42**, 3009-3016. https://doi.org/10.1161/strokeaha.110.610949

[103] Ziai, W., Moullaali, T., Nekoovaght-Tak, S., Ullman, N., Brooks, J.S., Morgan, T.C., *et al*. (2013) No Exacerbation of Perihematomal Edema with Intraventricular Tissue Plasminogen Activator in Patients with Spontaneous Intraventricular Hemorrhage. *Neurocritical Care*, **18**, 354-361. https://doi.org/10.1007/s12028-013-9826-1

[104] Hanley, D.F., Lane, K., McBee, N., Ziai, W., Tuhrim, S., Lees, K.R., *et al*. (2017) Thrombolytic Removal of Intraventricular Haemorrhage in Treatment of Severe Stroke: Results of the Randomised, Multicentre, Multiregion, Placebo-Controlled CLEAR III Trial. *The Lancet*, **389**, 603-611. https://doi.org/10.1016/s0140-6736(16)32410-2

[105] Huttner, H.B., Schwab, S. and Bardutzky, J. (2006) Lumbar Drainage for Communicating Hydrocephalus after ICH with Ventricular Hemorrhage. *Neurocritical Care*, **5**, 193-196. https://doi.org/10.1385/ncc:5:3:193

[106] Huttner, H.B., Nagel, S., Tognoni, E., Köhrmann, M., Jüttler, E., Orakcioglu, B., *et al*. (2007) Intracerebral Hemorrhage with Severe Ventricular Involvement: Lumbar Drainage for Communicating Hydrocephalus. *Stroke*, **38**, 183-187. https://doi.org/10.1161/01.str.0000251795.02560.62

[107] Staykov, D., Kuramatsu, J.B., Bardutzky, J., Volbers, B., Gerner, S.T., Kloska, S.P., *et al*. (2017) Efficacy and Safety of Combined Intraventricular Fibrinolysis with Lumbar Drainage for Prevention of Permanent Shunt Dependency after Intracerebral Hemorrhage with Severe Ventricular Involvement: A Randomized Trial and Individual Patient Data Meta-analysis. *Annals of Neurology*, **81**, 93-103. https://doi.org/10.1002/ana.24834

[108] Staykov, D., Huttner, H.B., Struffert, T., Ganslandt, O., Doerfler, A., Schwab, S., *et al*. (2009) Intraventricular Fibrinolysis and Lumbar Drainage for Ventricular Hemorrhage. *Stroke*, **40**, 3275-3280. https://doi.org/10.1161/strokeaha.109.551945

[109] Zhang, Z., Li, X., Liu, Y., Shao, Y., Xu, S. and Yang, Y. (2007) Application of Neuroendoscopy in the Treatment of Intraventricular Hemorrhage. *Cerebrovascular Diseases*, **24**, 91-96. https://doi.org/10.1159/000103122

[110] Li, Y., Zhang, H., Wang, X., She, L., Yan, Z., Zhang, N., *et al*. (2013) Neuroendoscopic Surgery versus External Ventricular Drainage Alone or with Intraventricular Fibrinolysis for Intraventricular Hemorrhage Secondary to Spontaneous Supratentorial Hemorrhage: A Systematic Review and Meta-Analysis. *PLOS ONE*, **8**, e80599. https://doi.org/10.1371/journal.pone.0080599

[111] Liu, N., Cadilhac, D.A., Andrew, N.E., Zeng, L., Li, Z., Li, J., *et al*. (2014) Randomized Controlled Trial of Early Rehabilitation after Intracerebral Hemorrhage Stroke: Difference in Outcomes within 6 Months of Stroke. *Stroke*, **45**, 3502-3507. https://doi.org/10.1161/strokeaha.114.005661

[112] Christensen, M.C., Mayer, S.A., Ferran, J. and Kissela, B. (2009) Depressed Mood after Intracerebral Hemorrhage: The FAST Trial. *Cerebrovascular Diseases*, **27**, 353-360. https://doi.org/10.1159/000202012

[113] Vermeer, S.E., Algra, A., Franke, C.L., Koudstaal, P.J. and Rinkel, G.J.E. (2002) Long-Term Prognosis after Recovery from Primary Intracerebral Hemorrhage. *Neurology*, **59**, 205-209. https://doi.org/10.1212/wnl.59.2.205

[114] Chapman, N., Huxley, R., Anderson, C., Bousser, M.G., Chalmers, J., Colman, S., *et al*. (2004) Effects of a Perindopril-Based Blood Pressure–lowering Regimen on the Risk of Recurrent Stroke According to Stroke Subtype and Medical History. *Stroke*, **35**, 116-121. https://doi.org/10.1161/01.str.0000106480.76217.6f

[115] Fandler-Höfler, S., Ropele, S., Gattringer, T., Haidegger, M., Pinter, D., Kneihsl, M., *et al*. (2025) Neuroimaging Markers Associated with Recurrent Stroke in Intracerebral Hemorrhage and Atrial Fibrillation. *Neurology*, **105**, e214386. https://doi.org/10.1212/wnl.0000000000214386

[116] Boulouis, G., Charidimou, A., Pasi, M., Roongpiboonsopit, D., Xiong, L., Auriel, E., *et al*. (2017) Hemorrhage Recurrence Risk Factors in Cerebral Amyloid Angiopathy: Comparative Analysis of the Overall Small Vessel Disease Severity Score versus Individual Neuroimaging Markers. *Journal of the Neurological Sciences*, **380**, 64-67. https://doi.org/10.1016/j.jns.2017.07.015

[117] Wan, S., Ji, X., Meng, R. and Li, M. (2025) Potential Therapeutic Targets and Emerging Strategies to Promote Hematoma Resolution in Intracerebral Hemorrhage. *Revista de Neurología*, **80**, Article 46121. https://doi.org/10.31083/rn46121

[118] Selim, M., Foster, L.D., Moy, C.S., Xi, G., Hill, M.D., Morgenstern, L.B., *et al*. (2019) Deferoxamine Mesylate in Patients with Intracerebral Haemorrhage (i-Def): A Multicentre, Randomised, Placebo-Controlled, Double-Blind Phase 2 Trial. *The Lancet Neurology*, **18**, 428-438. https://doi.org/10.1016/s1474-4422(19)30069-9

[119] Zhao, X., Song, S., Sun, G., Strong, R., Zhang, J., Grotta, J.C., *et al*. (2009) Neuroprotective Role of Haptoglobin after Intracerebral Hemorrhage. *The Journal of Neuroscience*, **29**, 15819-15827. https://doi.org/10.1523/jneurosci.3776-09.2009

[120] Leclerc, J.L., Li, C., Jean, S., Lampert, A.S., Amador, C.L., Diller, M.A., *et al*. (2019) Temporal and Age-Dependent Effects of Haptoglobin Deletion on Intracerebral Hemorrhage-Induced Brain Damage and Neurobehavioral Outcomes. *Experimental Neurology*, **317**, 22-33. https://doi.org/10.1016/j.expneurol.2019.01.011

[121] Cummins, D.D., Rifi, Z., Kalagara, R., Javin Bose, S., Agosto, K., Lefton, D., *et al*. (2025) Corticospinal Tractography and Motor Function in Patients Undergoing Intracerebral Hemorrhage Evacuation. *Stroke*: *Vascular and Interventional Neurology*, **5**, e001876. https://doi.org/10.1161/svin.125.001876

[122] Pradilla, G., Ratcliff, J.J., Hall, A.J., Saville, B.R., Allen, J.W., Paulon, G., *et al*. (2024) Trial of Early Minimally Invasive Removal of Intracerebral Hemorrhage. *New England Journal of Medicine*, **390**, 1277-1289. https://doi.org/10.1056/nejmoa2308440