

# 慢性硬膜下血肿联合治疗的时机与方式优化策略

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## 摘要

慢性硬膜下血肿(chronic subdural hematoma, cSDH)是神经外科常见疾病, 钻孔引流(burr hole drainage, BHD)术后复发率较高。脑膜中动脉栓塞术(middle meningeal artery embolization, MMAE)通过阻断血肿包膜血供, 为降低复发与再手术风险提供了新策略。本综述系统梳理了MMAE联合BHD或单独应用的优化证据: 联合治疗可降低复发风险约50%且不增加严重并发症, 但其获益因亚组而异; 术前栓塞可能降低再手术率, 同期联合可缩短住院时间; 液体栓塞剂渗透优势明显但成本高, 颗粒性价比更优; 经桡动脉入路对高龄患者有益; MMAE支持安全早期重启抗栓治疗, 他汀等辅助药物在现有研究中未显示额外临床获益。综上, MMAE联合BHD能有效降低cSDH复发与再干预风险, 但获益具有明显异质性, 未来需开展高质量研究明确最佳适用场景。

## 关键词

慢性硬膜下血肿, 脑膜中动脉栓塞, 钻孔引流, 联合治疗, 优化策略

# Timing and Method Optimization Strategies for Combined Treatment of Chronic Subdural Hematoma

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## Abstract

Chronic subdural hematoma (cSDH) is a common neurosurgical disease, and the recurrence rate after burr hole drainage (BHD) is high. Middle meningeal artery embolization (MMAE), which blocks the blood supply to the hematoma membrane, offers a new strategy to reduce the risk of recurrence and reoperation. This review systematically synthesizes evidence on the optimization of MMAE combined with BHD or as a standalone treatment: combination therapy reduces the recurrence risk by approximately 50% without increasing major complications, but the benefit varies by patient subgroup. Preoperative embolization may reduce the reoperation rate, while concurrent combination shortens hospital stay. Liquid embolic agents have advantages in penetration but are costly, whereas particles are more cost-effective. Transradial access is beneficial for elderly patients. MMAE supports safe and early resumption of antithrombotic therapy, while adjunctive drugs such as statins have shown no additional clinical benefit in existing studies. In summary, MMAE combined with BHD effectively reduces the risk of recurrence and reintervention in cSDH, but the benefit is markedly heterogeneous. Future high-quality studies are needed to define the optimal clinical scenarios for its application.

## Keywords

Chronic Subdural Hematoma, Middle Meningeal Artery Embolization, Burr Hole Drainage, Combined Treatment, Optimization Strategy

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## 1. 引言

cSDH 是一种常见的神经外科疾病, 在老年人颅内血肿较为常见[1]。对于有症状或占位效应明显的 cSDH 患者, 目前的标准治疗是手术清除, 通常采用 BHD [2] [3]。然而, 该方法存在较高的复发风险, 据报道, BHD 术后复发率约为 7.1%至 13%。在某些倾向性评分匹配队列中, 这一比例甚至高达 22.9% [1][4]。文献报道的再手术率在 12.7%或更高[5]。这种反复与再干预的循环会导致一系列不良后果: 住院时间延长、医疗资源消耗增加、总体成本上升, 同时也会增加不良功能结局和死亡风险[6][7]。综上所述, BHD 术后的复发风险构成了当前 cSDH 治疗的核心困境, 也凸显了寻求更有效降低复发策略的紧迫性。

尽管 BHD 对症状性 cSDH 的疗效已得到公认, 但其存在的复发风险, 影响相当比例的 cSDH 患者进行多次住院甚至多次手术。这迫使我们探索直接针对其潜在病理生理机制的辅助治疗策略。MMAE 代表一种创新技术。其作用原理是使维持慢性血肿扩张的富血管新生包膜去血管化, 从而抑制复发的炎症和血管生成因子[8]。在临床应用上, 该技术可通过两种互补的模式实施: 作为 BHD 的辅助手段以降低术后复发, 或者在严格选择的患者中作为传统手术的独立替代方案[9] [10]。MMAE 的临床前景得到了高级别证据的支持。例如, 荟萃分析显示, 与标准治疗相比, MMAE 可显著降低复发风险, 相对风险降低约 50%, 同时, 它也能相应减少再手术率[5] [11]。此外, 新的研究提示 MMAE 在特定高危人群中还具有额外优势。具体来说, 需要早期重启抗栓治疗的患者和老年衰弱患者, 其安全性和功能结局均得到改善[12]-[14]。因此, MMAE 代表了一种机制上合理且日益得到验证的策略, 用于应对 cSDH 复发的核心临床困境。

由于 MMAE 在降低 cSDH 复发和再手术风险方面的临床价值已有多项研究支持, 故当前研究的前沿

正从“是否有效”转向“如何优化”。但是在联合时机和实施细节上,仍存在关键证据空白[15]-[17]。具体而言, MMAE 与 BHD 的最佳协同时机仍存争议。例如, 单次麻醉下同期联合治疗是否优于分期策略? 术前栓塞还是术后栓塞效果更好? 术后早期( $\leq 2$  天)抑或延迟(3~7 天)栓塞对预后更有利? 这些问题均尚无定论[18]-[21]。此外, 技术与围术期实施策略同样面临诸多待解的临床选择。这包括: 栓塞材料(颗粒、液体还是弹簧圈)的选用[22]-[25]; 经桡动脉与经股动脉入路的安全性和疗效比较[26]-[28]; 全麻与非全麻的影响[29]; 抗栓治疗的安全重启时机; 以及他汀、皮质类固醇等辅助药物的潜在附加价值[30]-[36]。因此, 本综述并非简单重复 MMAE 的疗效, 而是系统梳理这些优化策略的证据。本研究的目标是为在不同临床场景下最佳的制定时机选择、技术执行和围术期管理, 提供基于现有证据的参考框架。

## 2. 联合治疗模式的临床价值验证与比较

### 2.1. 手术联合 MMAE vs 单纯手术

联合治疗的获益-风险比表现为疗效提升且未增加重大安全风险。就疗效而言, 联合治疗可降低复发与再手术率, 荟萃分析显示相对风险下降约 50% (如一项纳入 25 项研究、119,812 例患者的荟萃分析显示复发 RR = 0.47, 95%CI 0.36~0.62; 另一项 RCT 荟萃分析显示复发 RR = 0.47, 95%CI 0.34~0.65) [5] [8] [11], 该效应在 RCT 亚组分析、试验序贯分析及真实世界研究中表现出较好的一致性[37]-[40]。就安全性而言, 联合治疗不显著增加严重并发症及全因死亡率[8] [41]; 一项德国多中心研究(n = 718)报告症状性操作相关并发症发生率为 2.5% [42]。一项 GRADE 评估的荟萃分析提示感染率略高(8.4% vs 4.8%, RR = 1.81, 95%CI 1.23~2.66), 但该分析指出未转化为严重不良事件风险增加[5]。就功能结局而言, 联合治疗与单纯手术总体相当(荟萃分析显示功能独立 RR = 1.07, 95%CI 0.93~1.23), 一项前瞻性随机试验的中期结果甚至显示神经功能改善更优(P = 0.03) [43] [44]。

除降低复发率与再手术率外, 联合治疗还在部分研究中观察到影像学、医疗资源利用及特定抗栓场景下的多重改善, 但这些获益的幅度在不同结局指标上存在差异。第一, 在影像学改善方面, EMBOLISE 试验影像学研究显示, 联合治疗组术后 90 天和 180 天的血肿体积均显著小于单纯手术组(20.6 mL vs 28.9 mL, P = 0.03; 19.4 mL vs 31.5 mL, P = 0.04) [45]; 一项纳入 16 项研究的荟萃分析(n = 1814)也报告其能减少血肿厚度(SMD -0.17, P = 0.04)和中线移位(SMD -0.24, P = 0.01) [46]。第二, 在医疗资源利用方面, 联合治疗可降低再干预、随访及影像学检查需求。一项前瞻性随机试验显示, 单纯手术组需要更多的再干预(P = 0.02)、更长的随访(P = 0.02)和更多的影像学检查(P = 0.01) [43]; EMBOLISE 试验分析进一步表明, 未接受 MMAE 的患者非计划随访次数较联合治疗组增加近三倍(27.1% vs 14.7%, P = 0.0031) [47]。第三, 在抗栓管理高风险场景下, 一项大型多中心数据库研究显示, 对于需要早期抗凝的患者, 联合治疗组 6 个月死亡率(7.9% vs 19.4%, OR = 0.356, 95%CI 0.169~0.751)和再出血率(54.0% vs 66.9%, OR = 0.580, 95%CI 0.357~0.942)均低于单纯手术组[13]。

上述总体获益在不同患者亚组中存在值得注意的异质性——联合治疗的增量价值在高风险、占位效应明显的患者中可能性最大, 而病情较轻者可能仅需单独 MMAE。具体而言, 对于需要早期重启抗栓药物的患者, 联合治疗组 6 个月死亡率与再出血率显著更低[13], 且重启抗栓时间更早(8.5 天 vs 14 天) [12]; 一项倾向评分匹配研究显示, 在抗凝或抗板亚组中复发风险降低(OR = 0.72, 95%CI 0.322~0.746) [48]; 在老年衰弱患者中复发率从 19.8%降至 7.8% (P = 0.009) [12]; 在分隔型血肿患者中再手术率从 16.8%降至 0% (P = 0.006) [49], 另一项研究显示复发率仅为 3% (vs 无分隔组 16.7%, P = 0.017) [50]。与之相对, 对于血肿厚度为 16 mm、症状不重的低风险患者, 一项多中心倾向评分匹配研究单独 MMAE 与联合治疗的再手术率(7.8% vs 13.0%, P = 0.28)和影像学失败率相近[51]; 一项 RCT 荟萃分析也显示, 单独 MMAE 对

非手术患者的相对风险降低为 64% (RR = 0.36, 95%CI 0.22~0.60), 而作为手术辅助时相对风险降低为 35%(RR = 0.65, 95%CI 0.48~0.89), 提示获益幅度存在差异[38]。

补充上述临床获益, 从经济视角看, 联合治疗的初始成本较高, 其成本-效益结论因医疗体系而异, 提示需精准选择获益人群并优化围术期管理。在英国 NHS 体系中, MMAE 联合硬膜下引流(SEPS)的住院费用(£11,058.87)高于单纯 BHD (£7695.30) [52]; Jayakumar 等人的马尔可夫模型显示 MMAE 在该体系下“不适用于普遍使用”[7]。相反, 在单中心研究中, 尽管 MMAE 组再手术率为 0%(单纯手术组为 14%), 但其更高成本使单纯手术成为基础情景下的成本最小化选择[53]; 而 Tong 等人基于全国再入院数据库的马尔可夫模型却显示 MMAE 具有成本效益[54]。此外, 在残余复发风险方面, 即使接受联合治疗, 一项研究显示 MMAE 联合 BHD 术后复发率仍达 16.5%, 独立危险因素包括引流量少、无高压氧治疗、入院 GCS 低及术前血肿体积大[55], 提示联合治疗可能无法完全消除复发风险, 围术期管理细节至关重要。

## 2.2. 单独 MMAE vs 传统治疗

单独 MMAE 在多项研究与 cSDH 复发率及后续再手术率的降低存在关联。网络荟萃分析显示, 复发率降至传统手术的 0.12~0.51 倍[2] [9] [10]。这一发现在更接近临床实际的研究设计中同样可观察到: 一项倾向性评分匹配分析显示, 与 BHD 相比, MMAE 组的复发率更低(2.4% vs 14.6%,  $P = 0.048$ ), 治愈率更高(63.4% vs 41.5%,  $P = 0.047$ ) [56]。网络荟萃分析进一步提示, 单独 MMAE 优于单纯 BHD (OR = 0.37, 95%CI 0.23~0.58) [34]; 一项国家数据库研究则表明, 单纯 BHD 的复发率是 MMAE 的 2.11 倍(OR = 2.11, 95%CI 1.11~4.01,  $P = 0.020$ ) [3]。综上, 来自不同研究类型与人群的证据相互印证, 为单独 MMAE 作为降低复发率与再手术率的替代策略提供了依据。

在降低复发的同时, 单独 MMAE 的安全性及资源利用表现在多项研究中未明显劣于或优于传统手术。死亡率方面, 两者差异未达统计学显著性[2]; 在并发症方面则部分研究观察到 MMAE 的某些优势。一项全国性倾向匹配分析提示, MMAE 的神经并发症发生率低于手术(2.7% vs 7.1%,  $P = 0.029$ ), 且非常规出院率较低(53.8% vs 71.7%,  $P < 0.001$ ) [57]。另一项倾向评分匹配分析也指出, 手术出现并发症的几率约为 MMAE 的 1.8 倍(OR = 1.8,  $P < 0.0001$ ) [9] [58]。内科不良事件的风险差异更为突出: 一项研究报告 MMAE 组为 1.1%, 手术组为 15.2% (RR = 0.07,  $P = 0.013$ ) [59]。住院时间方面, 多项研究一致记录到 MMAE 组住院天数更短(中位或均值差异为 2~6 天) [56] [57] [59]; 其中一项数据库研究报告 MMAE 组中位住院时间为 0 天(IQR 0~1), 手术组为 6 天(IQR 5~7),  $P < 0.0001$  [6]。同时, MMAE 与较低的非常规出院率相关[57] [58]。综合来看, 单独 MMAE 在安全性与资源利用方面的数据, 支持其作为一线替代方案的可行性。

单独 MMAE 的潜在获益人群正在从传统意义上的保守治疗失败或手术高风险患者, 扩展至既往被认为需要常规手术干预的“大血肿”患者。对于非手术适应证人群, 荟萃分析及倾向评分匹配研究提示, 单独 MMAE 可使治疗失败风险降低约 64% (RR = 0.36, 95%CI 0.22~0.60; NNT = 4), 且后续手术需求降低 (OR = 0.472, 95%CI 0.235~0.946,  $P = 0.031$ ) [38] [60]。更重要的是, 在因血肿较大(厚度 > 15 mm 和/或中线偏移  $\geq 5$  mm)而被传统经验排除的患者中, 单独 MMAE 仍表现出一定的疗效: 再手术率为 7.6%, 88.9% 达到影像学缓解, 且疗效与较小血肿患者相比未见显著差异( $P = 0.87$  和  $P = 0.85$ ) [61]。这一现象在肿瘤患者中尤为明显: 相比手术引流, 单独 MMAE 组再手术降低 87.5% (IRR = 0.125, 95%CI 0.03~0.45,  $P = 0.001$ ), 且化疗恢复时间显著提前( $P = 0.005$ ) [62]。上述发现提示, 单独 MMAE 的临床应用可能不受到常规手术在血肿大小阈值的严格限制。

传统手术能够更快缓解早期占位效应, 但单纯 MMAE 在长期结局方面可能更具优势——其血肿消退速度虽较慢, 最终效果未明显劣于手术, 且复发率较低。现有证据表明, 手术组血肿的中位消退时间

约为 11 周, MMAE 组约为 14 周, 与开颅手术相比, MMAE 的消退时间更长( $P=0.03$ ), 但与 BHD 相比无显著差异( $P=0.12$ ) [63]。Housley 等人的倾向性匹配分析显示, 术后 24 小时及 3~12 周内, 手术组的血肿缩小量大于单纯 MMAE 组, 但远期随访未见显著差异; 而手术组的总体复发率(22.9%)高于 MMAE 组(4.2%,  $P=0.01$ ) [4]。此外, Falzon 等人的研究提示, 对于大血肿(厚度  $> 15$  mm), MMAE 的体积缩小效果更为明显(1~3 个月体积缩小  $63\text{ mm}^3$ ,  $P<0.001$ ) [64]。整体来看, 手术在早期血肿消退速度上的优势并未延续为更优的长期结局; 单纯 MMAE 虽起效较缓, 但在最终临床状态未见显著差异, 且复发风险更低。

### 2.3. 特定人群与卫生经济学

MMAE 治疗 cSDH 的临床获益在不同高危亚组中呈现显著异质性, 其价值在现有研究中高度集中于老年、分隔型血肿、肿瘤及大血肿等特定患者群体。高龄患者的获益尤为突出: 年龄  $\geq 80$  岁者接受 MMAE 后并发症率仅 5.8%、死亡率 1.2%, 且 81% 可直接出院 [14]; 年龄  $\geq 90$  岁的超高龄患者中, 单纯 MMAE 可使超过 90% 免于再次手术, 但血肿吸收速度相对较慢, 提示其虽能高效预防复发, 但对促进已有血肿吸收作用有限 [65]。对于合并抗凝治疗或身体虚弱的老年患者, 联合治疗仍可实现 86.0% 的良好功能结局 [52]。分隔型血肿患者从 MMAE 中的获益更为显著: 治疗后复发率仅为 3% (相较于无分隔组的 16.7%,  $P=0.017$ ) [50], BHD 联合 MMAE 可使再手术率从 16.8% 降至 0% [49], 提示分隔结构导致的复杂包膜血供可被 MMAE 有效阻断。肿瘤患者的获益体现在治疗连续性上: 相较于 BHD, MMAE 能显著缩短重启化疗的时间( $P=0.005$ ), 且无需血小板输注(手术组中位输注量为 6 单位), 中位住院时间也更短(3 天 vs 9 天), 表明 MMAE 可在控制血肿的同时避免延迟全身治疗 [62]。对于常规随机对照试验常予排除的大血肿(厚度  $> 15$  mm 或中线移位  $\geq 5$  mm)但神经功能稳定的患者, 单纯 MMAE 的再手术率仅为 7.6% [61]; Falzon 等人建议优先将 MMAE 用于血肿厚度  $> 15$  mm 或单侧血肿的 cSDH 可更快促进血肿吸收, 这可能说明大血肿本身不构成 MMAE 禁忌, 但其占位效应缓解较慢, 需审慎选择 [64]。

MMAE 治疗 cSDH 的成本效果因医疗支付体系而异, 但通过优化栓塞剂选择及手术入路等策略, 可在不降低疗效的前提下显著降低成本。基于某全国性数据库的分析显示, MMAE 具有可接受的成本效果: 增量成本效果比为 15199.8 美元 per QALY [54], John 等人的数据库分析显示单独 MMAE 的中位住院时间为 0 天 [6], 指数住院费用显著低于手术组; Salih 等人的一项匹配分析显示 MMAE 与开放手术的总住院成本无显著差异(71,569 美元 vs 60,598 美元,  $P=0.385$ ) [40], Findlay 等人指出当联合治疗成本低于 21,000 美元时可被视为成本最小化方案 [53]。相比之下, 在英国 NHS 下, MMAE 的普遍使用预计将导致净亏损 160 至 190 万英镑, “目前不具备成本效果” [7], 联合治疗的单次住院成本显著高于单纯 BHD (11058.87 英镑 vs 7695.30 英镑) [52]。为应对成本困境, 选择颗粒栓塞剂成为关键策略: Gajjar 等人的成本分析显示其材料成本仅为 152.74 美元, 远低于液体栓塞剂的 3703.17 美元( $P<0.0001$ ), 而两者在再治疗率和功能结局上无显著差异, 提示疗效等价前提下可直接节省大量耗材费用 [66]。同时, 采用经桡动脉入路联合清醒镇静在部分研究与缩短住院时间相关, 可能进一步降低医疗成本。

## 3. 联合治疗中手术与栓塞的协同时机优化

### 3.1. 单次麻醉同期联合 vs 分期治疗

单次麻醉下同期实施 MMAE 与 BHD 治疗症状性 cSDH, 在保持可接受安全性的同时, 部分研究显示显著提升了医疗效率 [16] [67]。具体而言, 相比分期操作, 同期联合可缩短总麻醉时间(从 225 分钟降至 165 分钟,  $P<0.001$ )和住院时长(倾向评分匹配后从 7 天降至 5 天,  $P=0.002$ ) [16] [17]; 且在同一框架下, BHD 较开颅手术的手术时间更短(190 vs 209 分钟,  $P=0.015$ )、引流管拔除更早、术后 6 日内出院率

更高( $P = 0.040$ ) [67]。重要的是, 这一效率提升并不伴随核心疗效的下降: 两组患者的血肿复发率、再手术率、功能结局及死亡率均无显著差异, 且同期策略的总体并发症风险(10.8%)与死亡率亦与分期治疗相当[16][17][67]。然而, 同期联合的效率优势并非绝对——Kim 等人的单中心研究显示, 在混合手术室中其时间指标并不总是优于分期方案, 提示该优势高度依赖设施配置与流程管理[68]。因此, 临床决策应基于自身条件审慎评估, 而非默认其普遍优越性。

### 3.2. 术前、术后及早期、延迟栓塞

关于 cSDH 行 MMAE 的最佳时机尚无统一结论。现有证据围绕术前与术后顺序、术后早期( $\leq 2$  天)与延迟(3~7 天)栓塞展开。一项倾向匹配分析显示术前栓塞组 6 个月再手术率显著低于术后栓塞组(7.1% vs 17.8%; OR = 0.35, 95%CI 0.17~0.71,  $P = 0.003$ ) [21]。然而, 一项大样本队列研究[15]未发现显著差异, 但另一项多中心回顾性研究承认对低于 11.6%的再手术率差异检验效能不足[20]——换言之, 该结论无法排除具有临床意义的 10.7%绝对风险差。同期(同一天)联合栓塞在再手术率、死亡率上与分期栓塞无显著差异, 但 Chen 等人报告可显著缩短住院时间(8 天 $\rightarrow$ 5 天,  $P < 0.001$ )并降低费用(约节省 1.1~1.2 万美元,  $P < 0.05$ ) [15], 是高效经济的备选方案。关于术后窗口, 早期( $\leq 2$  天)MMAE 相比延迟(3~7 天)MMAE 显示出死亡率降低趋势(6.1% vs 11.0%; OR = 0.527,  $P = 0.114$ ), 再手术率无差异[19]。综上, 术前栓塞可能为首选(基于再手术率优势); 术后早期栓塞有潜在死亡率获益, 同期栓塞则是兼顾疗效与经济效益的合理替代。

上述一般性结论需注意两项限定条件。其一, 复发性 cSDH 中较早行 MMAE 可能与增加再次复发风险相关: 栓塞后复发组距初次手术的时间间隔短于治愈组( $31.3 \pm 12.8$  天 vs  $63.9 \pm 38.9$  天,  $P = 0.039$ ), 且栓塞前复发间隔较短亦与栓塞后复发相关( $15 \pm 6.4$  天 vs  $30 \pm 22.1$  天,  $P = 0.023$ ) [18]。其二, 抗栓治疗构成重要混杂因素——在 cSDH 未完全消退前重启抗栓的患者, Chaliparambil 等人报告影像学消退率显著低于未重启组(21.9% vs 49.4%; OR = 0.2872, 95%CI 0.1113~0.7404,  $P = 0.0103$ ), 重启中位时间为术后 35.5 天[30]。这意味着, 延迟栓塞(如超过 30 天)的疗效评估易受抗栓重启干扰, 而术后早期( $\leq 2$  天)栓塞因发生在重启抗栓之前, 能提供更少混杂的评估窗口。因此, 未来比较栓塞时机的研究应将抗栓治疗作为分层变量或纳入排除标准, 抗栓管理本身也可能是优化联合治疗的重要干预靶点。

## 4. 精细化技术策略与围手术期管理

### 4.1. 栓塞材料与器械选择

现有证据表明, 各类栓塞材料均表现可接受的有效性和安全性, 在放射学改善、再手术率或主要并发症方面无显著差异。基于多项荟萃分析及一项纳入 1070 例的多中心倾向性匹配研究显示, 复发率(5%~7%)、再手术率(7%~12%)及主要并发症(约 2%~3%)在各组间均无统计学差异[22] [25] [69]。然而, 在这一总体等效性框架下, 不同材料在成本、操作效率和生物学渗透能力之间存在取舍关系。在成本、操作效率和生物学渗透性这三个维度上, 不同的栓塞材料展现出截然不同的优势分布, 临床决策中需进行明确的取舍。

液体栓塞剂具有生物学优势, 但代价是更高的材料成本和更长的操作时间。Salem 等人的多变量分析显示临床失败风险降低 68% (OR = 0.32, 95%CI 0.13~0.79,  $P = 0.011$ ) [70]; Sioutas 等人的荟萃分析提示再手术率降低 87% (RR = 0.13, 95%CI 0.02~0.95)见于液体栓塞剂的一线治疗[71]。穿透能力方面: Ganga 等人的研究显示 n-BCA 的脑膜穿透率达 55.1%, 优于 Onyx 的 17.0% ( $P < 0.0001$ ); 穿透越深、液体表面积越大, 血肿吸收越快[72][73]。Ma 等人的研究显示采用激进渗透策略后, 再手术率可降至 2.6% [74]。此外, Mortezaei 等人的 RCT 荟萃分析提示 n-BCA 与更低的全因死亡率相关( $P = 0.02$ ), 但需注意该结论基

于间接比较[75]。而在材料成本上, Gajjar 等人的成本分析显示液体栓塞剂约 3703 美元, 颗粒仅约 153 美元[66]。操作时间: Turnbull 等人报告单纯颗粒 55 分钟, 颗粒 + 弹簧圈 86 分钟( $P < 0.001$ ); Ashraf 等人报告单纯弹簧圈 34 分钟, 而 Onyx 需 63 分钟( $P < 0.001$ ) [23] [24]。值得注意的是, 技术简化并不损害疗效——Wang 等人和 Khorasanizadeh 等人的研究显示栓塞部位与分支数量在临床结局无显著差异[76] [77]。因此, 尽管液体剂在渗透与吸收方面可能具有上述优势, 颗粒与弹簧圈在资源受限或高手术量场景中展现出其独特的应用价值: 成本更低、效率更高、疗效无显著差异。

尽管各类栓塞材料的临床结局总体相当, 最佳选择需整合三个维度: 影像学标准、抗血小板药交互作用及个体化临床场景。第一, 影像学标准决定栓塞充分性。Ma 等人报告术后额顶支不显影可显著降低再手术率(3.3% vs 24%,  $P = 0.001$ )并加速血肿吸收[78]; 反之, Li 等人发现彩虹征持续或加重提示复发风险( $P < 0.001$ ), 要求材料具备远端渗透能力[79]。第二, 抗血小板药物管理方面, 延迟重启策略的适用性因材料而异。其依据在于: Patel 等人的多中心研究显示延迟重启( $\geq 3$  天)仅对颗粒栓塞亚组显著改善血肿厚度( $\beta = -8.3$  mm,  $P = 0.021$ ), 液体组无此关联( $\beta = 1.7$  mm,  $P = 0.773$ ) [31]。这一发现提示颗粒栓塞后需更严格遵循延迟策略。第三, 临床场景指导材料个体化选择。追求最低复发或再干预时, Ma 等人建议首选液体剂(尤其 n-BCA)联合激进渗透——再手术率可降至 2.6%。高手术风险或需快速操作时, Ashraf 等人和 Turnbull 等人的研究支持单纯颗粒或弹簧圈更具优势: 手术时间仅 34~55 分钟, 材料成本颗粒约 153 美元 vs 液体 3703 美元。资源有限环境下, 颗粒成本效益显著, 但其非劣效性有待 RCT 进一步证实。此外, 栓塞部位与分支数量在临床结局未见明显差异, 故个体化治疗才是关键。

## 4.2. 血管入路与麻醉管理

尽管经桡动脉入路(Transradial access, TRA)与经股动脉入路(Transfemoral access, TFA)在 cSDH 的 MMAE 中的总体安全性与疗效在荟萃分析中显示基本相当, 但针对高龄患者群体, TRA 因术后谵妄风险更低、住院时间更短而具有独特优势。首先, 一项系统综述与荟萃分析确认了两者在血肿复发率( $RR = 0.65$ , 95%CI 0.09~4.85)、手术时长( $MD = 0.04$  小时, 95%CI -0.49~0.56)、住院时长( $MD = 0.10$  天, 95%CI -0.11~0.31)及并发症方面的宏观等效性(如穿刺点并发症  $RR = 0.24$ , 95%CI 0.04~1.40) [26], 这为后续入路选择提供了参考。然而, 这种宏观等效性并未完全反映在高龄亚组中。一项大型多中心倾向评分匹配研究显示, 虽然 TRA 与 TFA 在并发症与功能结局上相当, 但 TRA 组手术时长更长(中位数 68.5 vs 59 分钟,  $P = 0.038$ ), 而 TFA 组影像学成功率更高(87.3% vs 77.4%,  $P = 0.036$ ) [28]。更关键的是, 该研究进一步揭示, TFA 组更常使用颗粒栓塞剂, TRA 组则更多应用 Onyx 胶( $P < 0.001$ ), 提示 TFA 在影像学上的优势很可能源于栓塞策略的差异, 而非股动脉入路本身的技术优势。而一项针对 $\geq 80$  岁患者(平均 83 岁, 其中 36% $\geq 90$  岁)的队列研究发现, TRA 与更短的住院时间显著相关[14]; 另一项针对术后谵妄的单中心回顾性研究更直接显示, TRA 组需要药物治疗的谵妄发生率显著低于 TFA 组(16.7% vs 46.2%), 且双侧手术的平均时间更短(151 vs 174 分钟) [27]。综上所述, 对于八九十岁的高龄 cSDH 患者, 可考虑优先选择桡动脉入路——它与降低谵妄风险、缩短住院时间相关, 尽管可能伴随手术时长的适度延长, 且需注意影像学成功率方面的表面劣势实则可能由栓塞材料选择的偏倚导致。

对于 cSDH 的 MMAE, 全麻与非全麻(如清醒镇静)的选择不影响主要临床结局。一项纳入 956 例手术的多中心研究显示, 两组在技术可行性、并发症、住院时长及功能恢复上均无显著差异, 且非全麻已占临床主流(70.4%) [29]。然而, 针对 80 岁以上高龄患者的荟萃分析发现, 全麻是延长住院时间的独立预测因子(校正后比值比 1.7, 95%CI 1.1~2.5), 年龄  $\geq 90$  岁者风险更高(aOR = 2.1, 95%CI 1.3~3.4) [14]。这提示全麻对年龄越高的人群可能带来更长的恢复期。综上, 麻醉方式应基于患者配合度、手术复杂性及医疗资源进行个体化选择, 而非依据疗效差异的假设。

### 4.3. 围术期抗栓与辅助药物

MMAE 为 cSDH 患者早期重启抗栓治疗创造了条件。首先, 总体证据支持其安全性与有效性: MMAE 本身可降低复发率并显著缩短抗栓中断时间(8.5 天 vs 14 天,  $P < 0.001$ ) [12]。Alkhiri 等人的汇总分析显示, 重启抗栓不增加出血并发症(重启组 14.1% vs 停药组 15.4%), 而停药组血栓事件风险显著升高(停药组 12.6% [95%CI 6.5~23.0] vs 重启组 3.5% [95%CI 1.8~6.9]), 复发率和再手术率无组间差异[32] [33]。进一步分析重启时机与栓塞剂类型: Patel 等人的研究显示术后第 3 天或更晚重启抗血小板可改善血肿厚度( $\beta = -5.7$  mm,  $P = 0.034$ ), 该获益仅见于颗粒栓塞亚组( $\beta = -8.3$  mm,  $P = 0.021$ ), 液体栓塞亚组无此效应( $\beta = 1.7$  mm,  $P = 0.773$ ) [31]。对于风险更高的抗凝人群: Lakhani 等人的多中心数据库研究显示, 需抗凝的高危患者中, 手术联合 MMAE 相比单纯手术可显著降低 6 个月死亡率(7.9% vs 19.4%,  $OR = 0.356$ , 95%CI 0.169~0.751,  $P = 0.005$ )和再出血率(54.0% vs 66.9%,  $OR = 0.580$ , 95%CI 0.357~0.942,  $P = 0.027$ ) [13]。综上, MMAE 在现有证据中支持安全、早期的抗栓重启(建议术后  $\geq 3$  天, 尤其颗粒栓塞后), 并为抗凝患者提供明确的生存与出血保护获益。因此, MMAE 围术期管理的核心应聚焦于安全重启抗栓治疗。

然而, 在 MMAE 的围术期管理中, 临床常会考虑联用辅助药物。与上述积极重启策略形成鲜明对比的是, 现有证据一致表明: 常规联用他汀、皮质类固醇或 Goreisan 等辅助药物并未显著改善临床结局, 部分药物甚至可能有害。关于他汀: Keil 等人的研究显示术前他汀暴露与复发无显著关联(6.4%总体复发率) [80]; Musmar 等人的荟萃分析显示 MMAE 联合他汀在血肿完全消退( $RR = 0.99$ , 95%CI 0.91~1.07)和复发率( $RR = 1.35$ , 95%CI 0.83~2.17)方面均不优于单纯 MMAE [81]; Musmar 等人的网络荟萃分析进一步支持他汀无额外获益, 且手术联合他汀反而复发率更高( $OR 3.08$ , 95%CI 1.77~5.36) [34]。这些发现共同表明, 他汀在 MMAE 基础上无额外获益, 甚至可能增加复发风险。关于皮质类固醇: Sioutas 等人的倾向评分匹配研究显示使用地塞米松的患者在 6 个月和 3 年时头痛发生率显著更高(21.2% vs 10.0%,  $P = 0.001$ ) [35]; Thakur 等人的研究显示在手术 + MMAE 患者中, 类固醇未改善主要结局, 反而有非显著的再入院率和死亡率升高[36]。关于 Goreisan: Akamatsu 等人的前瞻性队列研究显示在复发性 CSDH 中, BHD + Goreisan 基础上加用 MMAE 并未进一步降低再复发率(5.8% vs 5%,  $P > 0.05$ ) [82]。综上, 目前尚无高级别证据支持的辅助药物方案。这意味着, MMAE 围术期管理的核心, 仍应回归到安全、早期的抗栓重启策略上。

## 5. 结论与展望

BHD 联合 MMAE 在 cSDH 的治疗中展现了明确的临床价值。相较于单纯手术, 联合治疗在多项研究中显示可显著降低复发与再手术风险。对于 cSDH 患者, 单独 MMAE 作为替代方案, 其疗效在非劣效性分析中不劣于传统手术, 并体现出更短的住院时间和更少的内科并发症。总体而言, 基于 MMAE 的相关策略安全性可控, 未伴随主要操作并发症或死亡率的显著上升。

然而, 当前证据体系存在若干内在局限性, 需在解读结论时予以充分考虑。第一, 样本量有限, 且未针对多重比较进行校正, 存在假阳性风险。第二, 大多数研究的随访期较短(多为 90~180 天), 缺乏超过 1 年的长期随访数据, 无法评估远期复发模式、血肿完全吸收率及延迟性不良事件。第三, 不同研究间存在显著的异质性( $I^2$  范围 0%~89%), 体现在患者入选标准(血肿厚度、症状严重程度)、手术方式(BHD vs 开颅)、栓塞技术(材料、入路、渗透深度)、结局定义(复发标准、功能评估工具)及随访方案等多个维度, 这使得直接合并效应量和跨研究比较的可靠性受到限制。第四, 经济分析高度依赖特定医疗体系的定价结构和支付意愿阈值, 结论外推需谨慎。

由于联合治疗的增量价值存在亚组异质性且成本效果因体系而异, 将其转化为常规实践需审慎决策。采用联合方案的决策必须综合权衡操作风险、经济成本以及显著的患者间异质性, 因为联合 MMAE 的增

量价值在不同亚组中存在较大差异。此外, 在如何优化治疗策略方面仍存在显著的知识缺口——特别是在患者筛选标准、手术与栓塞的最佳时机与顺序、栓塞材料与血管入路的选择, 以及围术期管理方案的细化等方面。这些知识缺口提示, 需建立更精细的个体化决策框架, 而非采用统一推荐。

针对上述局限性, 未来研究应聚焦以下方向:

第一, 患者筛选与亚组 RCT。需开展前瞻性、具有充分把握率的亚组分析或针对特定人群的随机对照试验, 以明确不同亚组(如不同年龄分层、血肿影像学特征、抗栓需求)的获益 - 风险比。优先研究人群应包括需要长期抗凝治疗的患者、复发风险极高的分隔型血肿患者, 以及因肿瘤或合并症不适合手术的患者。

第二, 联合时机与栓塞材料的头对头研究。迫切需要进行高质量的头对头随机对照试验, 直接比较术前栓塞与术后栓塞、同期与分期策略, 以及不同栓塞材料(颗粒 vs n-BCA vs 弹簧圈)在真实世界中的长期疗效( $\geq 1$ 年)和成本 - 效果。关键终点指标应包括 180 天治疗失败率(复合终点, 含复发、进展、再手术)、功能独立率(mRS 0~2)、卫生经济学指标(成本 - 效用比), 并预设亚组分析以探索不同患者特征对治疗效果的修饰作用。同时应统一影像学评估标准(如采用体积评估而非仅厚度测量), 记录栓塞渗透深度等技术细节。

第三, 围术期抗栓重启的 RCT 及标准化登记系统。需开展设计严谨的随机对照试验或大型前瞻性队列研究, 明确抗血小板和抗凝药物在不同栓塞材料后的最佳重启时机(如术后第 1、3、7、14 天)。鉴于目前辅助药物均未显示获益, 不建议在常规实践中使用他汀、皮质类固醇或 Goreisan, 除非作为临床试验的一部分。此外, 建立国际多中心、标准化的 cSDH 登记系统, 统一收集基线特征、治疗细节、短期(90 天)和长期(1 年、2 年)结局, 以克服单中心研究的局限性, 提供更具外推性的证据。

总而言之, MMAE 代表了 cSDH 治疗领域的一项重要进展。尽管已有令人信服的证据支持其在降低复发与再干预风险方面的作用, 但该技术融入常规临床实践的最佳方式仍未完全明确。患者筛选、联合治疗的时机与技术执行、以及围术期管理等方面仍存在关键不确定性。填补这些空白需要开展高质量的比较研究(包括随机对照试验), 以明确 MMAE 在不同临床场景中的最佳角色——是作为手术清除的常规辅助手段, 还是高危亚组中的选择性补充, 亦或是经恰当选择患者中的独立替代方案。

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