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# 颅内未破裂微小动脉瘤的研究进展

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## 摘　要

**未破裂颅内微小动脉瘤(mini unruptured intracranial aneurysms, mUIAs)是指直径 ≤ 3 mm的颅内未破裂动脉瘤(unruptured intracranial aneurysms, UIAs)。目前对mUIAs的管理没有明确的指南。预防性手术干预可避免mUIAs自然破裂出血所造成的灾难性后果，但绝大部分mUIAs不会破裂。且目前无论采用哪种手术方式干预均非绝对安全。现对近年来关于mUIAs的文献进行综述，根据mUIAs的自然史、流行病学以及各种治疗方案的优劣势，来评估mUIAs是否需要手术干预。**

## 关键词

**颅内微小动脉瘤，未破裂，流行病学，自然史，治疗现状**

# Research Progress of Mini Unruptured Intracranial Aneurysms

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## Abstract

**Mini unruptured intracranial aneurysms (mUIAs) refer to unruptured intracranial aneurysms (UIAs) with a diameter ≤ 3 mm. There are no clear guidelines for the management of mUIAs. Prophylactic surgical intervention can avoid the catastrophic consequences of natural rupture hemorrhage of mUIAs, but most of mUIAs will not rupture. At present, no matter what kind of surgical treatment is not absolutely safe. This paper reviews the literature on mUIAs in recent years, and according to the natural history, epidemiology, and the advantages and disadvantages of various treatment options of mUIAs, evaluates whether mUIAs require surgical intervention.**

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**Keywords**

**Very Small Intracranial Aneurysm, Unruptured, Epidemiology, Natural History, Therapy Status**



## 1. mUIAs 的流行病学和自然史

研究表明直径 ＜7 mm 的颅内动脉瘤破裂风险很低[1]。但超过 50%的破裂动脉瘤直径 ＜5 mm [2]。二者之间的矛盾影响着 mUIAs 管理。

### 1.1. mUIAs 的流行病学

人群中颅内动脉瘤的发生率为 3% [3]，以往的研究报告称颅内动脉瘤发生率为 1%~2%，约占非创伤性蛛网膜下腔出血的 80%~85% [4]，随着影像学技术的不断进步和广泛使用，检测到无症状动脉瘤的数量已显著增加[5]。尸检研究表明动脉瘤在成年人中的患病率在 1%~5%之间[6]。其中 93%UIAs 直径 ＜10 mm，66%直径 ＜ 5 mm [3]。且 50%~80%的 UIAs 不会破裂[6]。日本未破裂颅内动脉瘤研究和未破裂颅内动脉瘤国际研究(International Study of Unruptured Intracranial Aneurysms，ISUIA)研究表明，在所有 UIAs 中，直径 ＜7 mm 的 UIAs 分别占 62.0%和 74.5% [1] [7]。国内人群行头部 MR 血管成像(MRA)筛查，动脉瘤发生率为 7%，其中微小动脉瘤占 40.7% [8]。Gupta 等[9]和 Lee 等[10]曾报道，微小动脉瘤占所有破裂动脉瘤总数分别是 7%和 15%。可增加动脉瘤破裂风险的可变因素包括吸烟、饮酒和高血压，不可变因素包括性别和年龄[11]。动脉瘤性蛛网膜下腔出血女性较男性多见(2:1)，50~60 岁为发病高峰[12]。但有研究者认为直径 ＜5 mm 的颅内动脉瘤年龄 ＜50 岁破裂风险显著增加[13]。

### 1.2. mUIAs 的自然史

据报道，颅内动脉瘤的年破裂率为 0.95% [13]，直径 ＜5 mm 的为 0.5%，直径 3~4 mm 的为 0.36% [14]。Morita 等[15]研究表明在日本人群中直径 ＜ 5 mm 的动脉瘤在大脑中动脉和前交通动脉的年破裂率分别为 0.23%和 0.9%。直径 ≤7 动脉瘤的生长和破裂之间存在正相关关系[16]，不稳定动脉瘤的破裂率为 3.1%，而稳定动脉瘤的破裂率为 0.1% [17]。Chien 等[18]研究发现直径 ≤5 mm 动脉瘤的年增长率为 5.10%，直径 ≤3 mm 动脉瘤的年增长率为 11.64%。Wermer 等人[19]报道，直径 1~3 mm 的动脉瘤在随访 1.3 年后 8.7%会增长或破裂。最近的一篇荟萃分析显示，直径 ＜ 5 mm 动脉瘤随访期间总体生长率和破裂率分别为 6.0%和 0.4% [20]。Sonobe 等[21]报道了单个和多个未破裂小动脉瘤的年破裂率为 0.34%和 0.95%，微小动脉瘤的年增长率为 1.22%和破裂率 0.23%。ISUIA 研究报告直径 2~7 mm 动脉瘤 5 年累积破裂率，无 SAH 和有 SAH 病史的前循环动脉瘤分别为 0%和 1.5%，后循环动脉瘤为 2.5%和 3.4% [1]。

## 2. mUIAs 的治疗现状

### 2.1. 保守治疗

#### 2.1.1. 随访

直径 ＜7 mm 的动脉瘤年破裂率低于 1.0% [22]，因此，对于动脉瘤直径 ＜7 mm 的患者，很多人推

荐保守治疗，定期复查评估动脉瘤大小和形态变化[13]。动脉瘤的生长和形态变化可以很好的预测动脉瘤的破裂，生长动脉瘤破裂风险是稳定动脉瘤的 5~55 倍，因此有研究者提出根据随访期间动脉瘤是否生长和形态变化来决定是否需要手术干预[23] [24] [25]。但是目前对 mUIAs 监测的首选成像技术、监测的频率和持续时间以及评估动脉瘤生长和破裂风险的最佳成像标准还没有达成共识。在一个调查研究中，选择对直径 < 7 mm 动脉瘤进行终生随访、随访 10 年、5 年和 2 年的医师占比分别为 59%、8.5%、21%和 12% [26]。定义小动脉瘤生长最常用的标准是至少在 1 个方向上生长 > 1 mm [26]。核磁血管造影(MRA)被认为是<7 mm 动脉瘤最好的随访方式，因为它既不涉及电离辐射也不涉及血管造影[27]。但是 MRA 在检测微小动脉瘤大小或形态特征的微小变化方面敏感性低[28]。此外，MRA 假阳性可能需要数字减影血管造影术进行确认。动脉瘤的生长是非线性的，通常具有较长的稳定期和短暂的动脉瘤生长期，准确和及时判断动脉瘤是否破裂有难度[29]。临床工作中患者一旦被确诊，将面临重大的心理压力、长期随访的经济负担、辐射或有创操作等，并且不能彻底解决动脉瘤破裂的可能性，每个动脉瘤都有其独特的特征，因此对每位患者或动脉瘤都需个体化处理。

#### 2.1.2. 药物治疗

动物模型和人体标本研究数据均表明，慢性炎症是颅内动脉瘤形成、进展和破裂的关键[30]。阿司匹林被称为抗炎药。研究表明，阿司匹林能减慢动脉瘤生长和减低破裂率，这可能与它对动脉瘤壁的抗炎作用有关[31] [32] [33]。Zanaty 等[34]在 Neurosurg 上发表文章称阿司匹林可显著降低动脉瘤的生长速度。Hasan 等[35]使用了 ISUIA 的数据，对 1691 名未破裂颅内动脉瘤患者进行了前瞻性随访，他们根据 58 名动脉瘤破裂患者服用阿司匹林的频率分析了蛛网膜下腔出血的风险，并与 213 名匹配的对照组(未服用阿司匹林的患者)进行比较，结果显示每周服用阿司匹林 ≥ 3 次的患者出血的优势比为 0.40 [95% CI = 0.18~0.87]，对照组优势比为 0.80 (95% CI = 0.31~2.05)，在多变量危险因素分析中，与从不服用阿司匹林的患者相比，每周或每天服用阿司匹林 ≥3 次的患者出血几率显著降低(OR = 0.27，95% CI 0.11~0.67，p = 0.03)。然而，Pottegard 等[31]证明短期(<3 个月)使用阿司匹林与动脉瘤破裂风险增加有关。研究发现，他汀类药物可通过增加一氧化氮和抑制巨噬细胞和平滑肌细胞中的促炎细胞因子、基质金属蛋白酶和一氧化氮合酶的多效性作用来保护内皮[36]。在实验性脑动脉瘤模型中他汀类药物具有保护作用，可以防止动脉瘤破裂[37]。然而，Bekelis 等[38]将 28,131 名 UIAs 患者随机分为他汀药物治疗组和非他汀药物治疗组，结果显示他汀类药物组的死亡率较低，但不能降低动脉瘤破裂风险。最近一项前瞻性研究也得出了同样的结果[39]。阿司匹林、他汀类药物治疗动脉瘤都是为了阻止动脉瘤生长来降低动脉瘤破裂的风险。但有报道称，56%的动脉瘤破裂发生在非生长的动脉瘤中[13]。吸烟、后循环、年龄和女性也是 UIAs 破裂的危险因素[5] [7]。动脉瘤生长并不是动脉瘤破裂的唯一危险因素。这两类药物是否能降低动脉瘤破裂风险还需要进一步研究。

### 2.2. 手术干预

有报道称，动脉瘤破裂死亡率接近 60%，且大部分幸存者存在神经功能缺损[40]。因此越来越多的神经外科医生支持对 mUIAs 进行手术干预[41]。

#### 2.2.1. 开颅显微外科治疗

颅内微小动脉瘤瘤体较小、瘤壁薄、瘤颈宽，显微手术具有较高的风险，术中出现瘤颈夹闭不全、瘤体破裂出血、误夹载瘤血管及穿支血管等均会导致不良后果[42]。在一项多中心国际研究中提到手术夹闭 mUIAs 的完全闭塞率为 98.2%，死亡率为 0%，永久性神经功能缺损并发症率为 2.7%，大脑中动脉远端至大脑中动脉 M1 段的动脉瘤是手术夹闭最安全部位，术后早期神经功能缺损的发生率为 6.3%，出现

神经功能障碍的患者动脉瘤大部分位于后循环，特别是位于基底动脉顶端的动脉瘤[43]。Bruneau 等[43]对 183 例经开颅夹闭、双极电凝或包裹 mUIAs 患者的临床资料进行分析，完全闭塞率达 98.2%、死亡率 0%和永久性神经功能缺损发生率为 2.7%，前循环动脉瘤和后循环动脉瘤手术后早期出现神经功能缺损的发生率分别为 3.9%和 45.5%。近年，Kiran 等[44]提出了一种新技术，术中将两个动脉瘤夹相互平行释放夹闭微小动脉瘤(双夹技术)，他们使用双夹技术夹闭 40 个微小动脉瘤，术后立即造影 39 个动脉瘤完全闭塞，1 个动脉瘤部分瘤颈残留，手术相关死亡率和致残率为 0%。宗钢等[45]回顾性分析使用双夹技术治疗的 24 例微小动脉瘤患者的临床资料及随访资料，认为双夹技术治疗微小动脉瘤的效果满意，具有较高的围手术期安全性，以及较高的短期治愈率和临床预后良好率。

#### 2.2.2. 血管内介入治疗

介入治疗具有微创、高效、安全等特点，成为了颅内动脉瘤主要治疗方法[46]。但血管内介入治疗微小动脉瘤也具有很大挑战，栓塞过程中微导管难以到位并固定于瘤腔，弹簧圈难以在瘤腔内成篮，更严重的是微导管或弹簧圈轻微的意外移动就有可能刺破动脉瘤[47]。第一个针对微小动脉瘤血管内治疗的大型研究显示手术相关破裂率为 11%，是较大动脉瘤的 5.2 倍[48]。随着手术医师的技术提高，更小、更软弹簧圈的改进，这一数据降到了 1% [49]。

#### 2.2.3. 单纯弹簧圈栓

单纯弹簧圈栓塞是治疗动脉瘤最常用和有效的方法[50]。2011 年，Hwang 等[51]也发表了一组关于微小动脉瘤介入治疗的数据，其结果显示，20 例未破裂动脉瘤中仅有 1 例(5%)发生术后并发症，手术致残、致死率均为 0，体现了相对较佳的疗效。近期，有荟萃分析发现单纯弹簧圈栓塞 mUIAs 是有效的，术后立即血管造影动脉瘤闭塞率 > 90%，出院时 82%的患者神经系统功能良好，6 个月后复查神经系统功能良好达 79% (95% CI，64%~89%) [52]。

#### 2.2.4. 支架辅助弹簧圈栓塞

颅内微小动脉瘤具备瘤体小、瘤壁薄和瘤颈宽等形态特点，导致其手术难度明显增大[53]。其血管内治疗常需要支架辅助。国内可选择的支架种类很多。其中低剖面可视化腔内支撑装置(low-profile visualized intraluminal support, LVIS)是一种新型的颅内自膨镍钛材料、闭环编织支架，具有良好的通过性、柔顺性和贴壁性，还可有效防止小的弹簧圈突出到载瘤动脉、重塑动脉瘤颈和血流分流等功能[54]。虽然致密网状支架与传统支架相比有很多优势，但致密支架也增加了动脉瘤附近分支动脉闭塞的可能性以及更容易形成血栓[55]。一项对 9 个研究的荟萃分析报告，LVIS 支架治疗的总体手术相关并发症发生率为 6.5%，血栓事件发生率为 4.9% [56]。尹佃敏等[57]回顾性分析 LVIS 支架辅助栓塞的 36 例颅内破裂微小动脉瘤患者的临床资料，术后即刻造影显示，Raymond 分级 I 级栓塞 83.3%，II 级栓塞 13.9%，III 级栓塞 2.8%，随访 5~12 个月后 mRS 评分显示，0 分 33 例，1 分 2 例，2 分 1 例，随访期间无死亡病例，表明使用 LVIS 支架辅助栓塞颅内破裂微小动脉瘤能提高动脉瘤的栓塞率，降低远期复发率。

#### 2.2.5. 血流导向装置(Flow Diverter, FD)

2007 年，Cekirge 及 Moret 在欧洲世界神经外科和神经介入会议上首次介绍了血流导向装置这一新的技术理念[58]。目前国内用的比较多的三种血流导向装置是 Silk 支架、Pipeline 栓塞装置和 Tubridge 血流导向装置。其中 Pipeline 栓塞装置和 Silk 支架用于治疗 mUIAs 有高的成功率和低的并发症已经被证实[59] [60] [61]。Chalouhi 等[62]使用 Pipeline 栓塞装置栓塞 100 例直径 ≤7 mm 的动脉瘤，85%完全或几乎完全闭塞，与手术相关的并发症发生率为 3%，结论显示 Pipeline 栓塞装置具有并发症少和和闭塞率高等优点。Tubridge 血流导向装置即是基于血流重构理念并由中国自主研发的新型 FD 系统。Liu 等[63]应用 Tubridge

血流导向装置治疗复杂动脉瘤的前瞻性多中心随机对照研究结果显示，Tubridge 治疗组术后 6 个月的完全闭塞率达 75.3%，显著高于支架辅助弹簧圈栓塞组的 24.5%，优势比为 9.4 (95%置信区间，4.14~21.38；P < 0.001)。吕楠等[64]回顾性分析应用 Tubridge 血流导向装置治疗的 139 例患者(共 143 个颅内动脉瘤)，对其临床及影像学资料进行分析，发现其在治疗颅内动脉瘤的技术成功率高、并发症少，临床应用安全可靠。综上所述，血流导向装置有可能成为治疗 mUIAs 主流方式之一。但目前血流导向装置仍处于起步阶段；缺乏长期、大量的实验数据支撑。以及血流导向装置会带来一些传统血管内技术不会遇到的并发症，如远端脑实质出血、装置的延迟迁移和术后迟发动脉瘤破裂[65]。远端实质出血可发生在动脉瘤的同侧或对侧，其机制可能与双重抗血小板聚集药物的使用和远端动脉的自动调节功能丧失有关[65]。大约 1%的患者在术后发生延迟性动脉瘤破裂，基于计算机模拟的血流动力学分析显示，在置入 FD 后瘤内压力增高，提示在 FD 置入后短期内存在着血流动力学与血栓形成之间相互作用的过程，其不平衡性可能是术后迟发破裂的潜在机制[65]。想代替常规血管内治疗 mUIAs 还需要大量的随机试验来证明其高闭塞率和低并发症。

## 3. 总结

随着影像学和介入学技术的进步，越来越多的无症状或轻微症状的颅内未破裂动脉瘤被检查出来。mUIAs 是手术治疗还是保守观察，目前仍然争议较多且缺乏精确有效的数据。对 mUIAs 的管理是非常复杂的，需要考虑动脉瘤的流行病学、自然病程、动脉瘤 SAH 个人史或家族史、吸烟、动脉瘤位置和动脉瘤进展等相关破裂危险因素，以及干预的风险和困难。

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