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烟雾病临床治疗及术后并发症预测研究进展

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摘　要

烟雾病是一种严重困扰成人尤其是儿童发育的慢性脑血管疾病。临床现有治疗方法多以手术为主，辅以内科及中医治疗。但术后并发症的高发病率以及难预料性仍给予临床工作一定的困难。本文回顾了近年来国内外烟雾病临床治疗方法及预后评价，发现术后并发症的预测应作为烟雾病临床治疗的一个重要方向。围手术期的管理及监测有望成为提前预防及干预术后并发症的重要措施。

关键词

烟雾病，临床治疗，围手术期

Advances in Clinical Treatment and Postoperative Complication Prediction of Moyamoya Disease

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Abstract

Moyamoya disease is a chronic cerebrovascular disease that seriously affects the development of

adults, especially children. The existing clinical treatment methods are mostly surgery, supplemented by internal medicine and traditional Chinese medicine. However, the high incidence and unpredictability of postoperative complications still make clinical work difficult. This paper reviewed the clinical treatment methods and prognosis evaluation of moyamoya disease at home and abroad in recent years, and found that the prediction of postoperative complications should be an important direction of clinical treatment of moyamoya disease. Perioperative management and monitoring are expected to be an important measure for early prevention and intervention of postoperative complications.

Keywords

Moyamoya Disease, Clinical Treatment, Perioperative Period

1. 引言

烟雾病(Moyamoya disease, MMD)是一种慢性脑血管疾病。由于受累血管造影图像形似"烟雾"而得名[1]。该病主要累及颈内动脉(ICA)末端，致使近端动脉代偿发育，少数病例也会累及到后路血管，包括大脑后动脉和脑基底部网状血管。其主要特征为受累血管的进行行狭窄与闭塞，进而导致大脑灌注不足，从而使得患者出现各种以脑缺血为表现的其他临床疾病，如缺血性脑卒中、癫痫发作、认知障碍、躯体功能障碍、残疾甚至是突发死亡[2]。

中国地区烟雾病发生率为 0.59/100,000 [3]，明显高于日本[4]及欧美国家[5]。该病可发生于各年龄阶段，但 5~19 岁及 40~59 岁为发病高峰期[6]。

烟雾病经治疗后能明显改善患者脑部血供，同时能有效预防 MMD 的缺血性并发症，但是术后疾病再发、中风、出血或水肿等不良反应依旧存在，患者整体预后不容乐观。这些术后不良事件的发生，在很大程度上与围手术期的管理不善有关，因此，本文就烟雾病近年来临床治疗方法以及预后评估指标进行系统性综述，为下一步开展 MMD 围手术期管理策略研究提供基础。

2. MMD 临床治疗方法

2.1. 内科对症治疗是 MMD 的辅助治疗手段

烟雾病的治疗与其疾病严重程度[7]和并发合并症相关。针对有癫痫、头痛、脑梗或出血的患者，临床医生可使用药物对症治疗。尤其急性梗死或轻度 MMD 患者，推荐使用药物治疗，以防止中风发生或复发[8]，但需注意，单一的药物治疗并不能完全缓解患者病情发生与发展。

2.2. 手术血管重建是 MMD 治疗的首选方法

烟雾病患者的 5 年生存率约为 96.1%，手术组与非手术组无明显差别。但是，烟雾病所导致的认知功能及躯体功能障碍，严重影响到患者生活质量。尤其是学龄前儿童患者，若不及时治疗，其认知水平会明显下降。烟雾病主要治疗方式是外科手术干预[9]，将颅内血管重建以期达到改善大脑低灌注，防止中风发生的效果，尤其对于儿童患者，在发生可逆性脑损伤之前，积极手术干预对其恢复正常大脑功能有着显著作用[10]。研究表明，烟雾病患者在接受手术治疗后，大约 80%的患者大脑半球的脑氧代谢显

著降低，在搭桥手术后无实质病变的儿童和年轻成人患者中，这一情况可以得到改善[11]。因此，手术成为了治疗 MMD 的首选方法。

MMD 手术适应指征详见《烟雾病及烟雾病综合征诊断与治疗中国专家共识(2017)》和《烟雾病治疗中国专家共识(2019)》。

2.2.1. 临床常用手术方式

1) 直接血管重建：颞浅动脉(STA) – 大脑中动脉(MCA)吻合术[12]，脑前动脉(ACA)吻合[13]，枕动脉(OA) – 大脑后动脉(PCA)吻合术[14]；2) 间接血管重建包括：脑 – 硬脑膜 – 动脉血管融合术(EDAS) (多用于儿童) [15]、脑一肌肉血管融合术(EMS) [16]、脑 – 硬脑膜 – 动脉 – 肌肉血管融合术(EDAMS) [17]，多点钻孔术[18]等。3) 联合手术。尽管有研究表明联合手术相较于其他单一手术方式获益更大[19]，但由于缺乏临床前瞻性研究验证，《烟雾病治疗中国专家共识(2019)》未将联合手术列为推荐方式。

2.2.2. 受损血管位置及程度以及血流动力学决定手术方式

临床上，患者具体采用哪种手术方式，应根据受损血管的位置情况和血流动力学而定。一般情况下，需要考虑以下三方面：1) 烟雾病类型，主要考虑出血性与缺血性以及分期大于 II 级；2) 患者年龄及耐受情况，尤其对于儿童患者来说，其颞浅动脉(STA)直径 < 0.7 mm，直接血管重建能够起到很好的效果；3) 血管选择，应尽量选择生理性血管，而不建议选择代偿血管。同时需要考虑供血血管的直径；4) 患者脑氧饱和度情况，术前应进行评估，术中实时监测以及术后持续性监测，以保证围手术期的安全和提高手术成功率。

综上，患者手术方式并不是一成不变的，应综合各类情况及时调整。

2.3. 中医治疗任重道远

除了外科手术及西药治疗外，我国有大量中医辅助治疗 MMD 病例报道，提示中医在临床应用过程中对 MMD 存在积极作用，但缺少大样本临床对照试验能支持其治疗结果，中医治疗 MMD 依旧任重而道远。

3. 术后并发症及预测

尽管手术血管重建能改善大脑血供，在儿童患者中更是可以降低远期中风风险，但是，手术作为一种干预措施，依旧诸多并发症，主要包括感染、出血、过度灌注综合征以及即时脑梗。因此患者的围手术期管理十分重要，如何降低围手术期风险、减少手术并发症、维护术后患者大脑氧供功能状态，成为重点关注的问题。

3.1. MMD 手术患者术后常见并发症

根据临床报道显示，MMD 术后的并发症主要有 TIA、缺血性脑卒中、脑表面出血、高灌注综合征以及神经功能障碍[20] [21] [22] [23] [24]等。儿童 MMD 患者术后易哭闹，情绪不稳定，加之过度换气，极易引起手术血管收缩从而引起不良的缺血性事件[25]。约 15%~27.5%成人患者会出现大脑过度灌注综合征，该综合征可导致短暂或永久性的神经功能缺损[20] [26]。临床上由于高灌注导致的神经功能障碍的发病时间从手术后即刻到 10 天不等[27] [28]，因此，在术后，准确监控患者脑灌注情况和血压情况，可早期识别患者血流动力学稳定情况及受损程度，对于烟雾病患者的术后管理至关重要。

3.2. 术后并发症的预测

2017 年日本富山医科药科大学神经外科学系 Daina Kashiwazaki 团队经研究发现，柏林分级评分系统在对成人 MMD 临床严重程度分级的同时，可用于预测其术后神经系统并发症的发病率。近期有研究认

为术前高血小板水平与术后过度灌注综合征密切相关[29]。其他相关研究多基于影像学基础之上，主要为高 MRA 评分与术后不良并发症有关[30] [31]。此外，有研究表明，术中及术后的脑电监测有助于预警患者即将出现的脑缺血状态[25]。术后行动脉自旋标记(ASL)灌注亦有助于早期诊断及发现过度灌注综合征[32]。我国有研究认为，术中使用包括 rSpO2 (脑氧饱和度)及 SVV (每搏变异率)的多模式监测分次测量可用于指导围手术期患者氧合及液体管理，也能有效降低术后谵妄和恶心呕吐的发生率[33]。

综上可知，患者术后是否具有高风险并发症发生，其本质上是与基础疾病严重程度相关。现阶段研究缺少在术中对患者的即时监控类研究，无法判断患者术后的不良反应是否是由手术本身所引起，所以围手术期患者持续性血氧水平监测有望成为预测患者预后的良好指标。

3.3. 围手术期用药策略

围手术期尤其是在术后，患者用药主要原则为对症治疗。有研究表明，在术后给予他汀类药物，能有效降低循环胆固醇，诱导内源性细胞增殖，促进血管生成，增加局部脑组织供血，从而起到保护血管内皮作用[34]。其次，围手术期给予阿司匹林及肝素能有效降低术后继发血栓形成[35]。针对 MMD 可能伴发的糖尿病或高血压等，也应积极处理，使患者术后获益最大化。

4. MMD 患者预后评价指标

总体来说，MMD 患者术后预后评价指标主要为，是否于围手术期发生缺血或出血等不良事件[36] [37]。除此之外，生活质量评估应该是预后评估的核心。尽管本病发生率不高，但极易导致儿童渐进性功能和认知障碍，从而导致生活质量受损、无法适应社会生活。因此，患者可能需要长期的心理支持治疗。

5. 小结

烟雾病是脑血管神经科学领域一类严重疾病，尤其是其可以导致儿童智力下降以及认知障碍，严重者会直接因为出血或缺血性脑梗死而死亡。早期诊断和及时治疗是降低该病死亡率的必要措施。

尽管烟雾病发病机制研究尚不完全清楚，但其临床治疗方法已经趋于成熟，外科治疗辅以内科药物可以有效降低患者再缺血的发生率。然而，在以外科为主导的治疗体系中，如何优化手术方案，做好围手术期监测，以及减少麻醉药物、手术方式对患者的潜在影响，也有待于进一步临床试验进行证实。

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参考文献

[1] Suzuki, J. and Kodama, N. (1983) Moyamoya Disease—A Review. *Stroke*, **14**, 104-109. https://doi.org/10.1161/01.STR.14.1.104

[2] Shang, S., Zhou, D., Ya, J., *et al.* (2020) Progress in Moyamoya Disease. *Neurosurgical Review*, **43**, 371-382. https://doi.org/10.1007/s10143-018-0994-5

[3] Sun, Y., Zhou, G., Feng, J., *et al.* (2021) Incidence and Prevalence of Moyamoya Disease in Urban China: A Nationwide Retrospective Cohort Study. *Stroke and Vascular Neurology*, **6**, e000909. https://doi.org/10.1136/svn-2021-000909

[4] Hoshino, H., Izawa, Y. and Suzuki, N. (2012) Epidemiological Features of Moyamoya Disease in Japan. *Neurologia Medico-Chirurgica*, **52**, 295-298. https://doi.org/10.2176/nmc.52.295

[5] Nisiewicz, M.J., Roberts, J.M., Dobbs, M.R., *et al.* (2020) High Prevalence of Moyamoya Syndrome in Appalachia. *Cerebrovascular Diseases*, **49**, 516-521. https://doi.org/10.1159/000510750

[6] Ahn, I.M., Park, D.H., Hann, H.J., *et al.* (2014) Incidence, Prevalence, and Survival of Moyamoya Disease in Korea: A Nationwide, Population-Based Study. *Stroke*, **45**, 1090-1095. https://doi.org/10.1161/STROKEAHA.113.004273

[7]   Suzuki, J. and Takaku, A. (1969) Cerebrovascular "Moyamoya" Disease. Disease Showing Abnormal Net-Like Vessels in Base of Brain. *Archives of Neurology*, **20**, 288-299. https://doi.org/10.1001/archneur.1969.00480090076012

[8]   Onozuka, D., Hagihara, A., Nishimura, K., *et al*. (2016) Prehospital Antiplatelet Use and Functional Status on Admission of Patients with Non-Haemorrhagic Moyamoya Disease: A Nationwide Retrospective Cohort Study (J-Aspect Study). *BMJ Open*, **6**, e009942. https://doi.org/10.1136/bmjopen-2015-009942

[9]   Mayeku, J. and Lopez-Gonzalez, M.A. (2020) Current Surgical Options for Moyamoya Disease. *Cureus*, **12**, e11332. https://doi.org/10.7759/cureus.11332

[10]   Ando, T., Shimada, Y., Fujiwara, S., *et al*. (2020) Revascularisation Surgery Improves Cognition in Adult Patients with Moyamoya Disease. *Journal of Neurology*, *Neurosurgery*, *& Psychiatry*, **91**, 332-334. https://doi.org/10.1136/jnnp-2019-321069

[11]   Ang, P., Cai, H., Luo, R., *et al*. (2021) Assessment of Surgical Outcomes in Children and Adult Ischemic Moyamoya Disease and Its Relationship with the Pre-Infarction Cerebral Perfusion Status. *Turkish Neurosurgery*, **32**, 43-51. https://doi.org/10.5137/1019-5149.JTN.33210-20.2

[12]   Taniguchi, M., Taki, T., Tsuzuki, T., *et al*. (2007) EC-IC Bypass Using the Distal Stump of the Superficial Temporal Artery as an Additional Collateral Source of Blood Flow in Patients with Moyamoya Disease. *Acta Neurochirurgica*, **149**, 393-398. https://doi.org/10.1007/s00701-006-1098-5

[13]   Egashira, Y., Yoshimura, S., Enomoto, Y., *et al*. (2018) Single-Stage Direct Revascularization for Bilateral Anterior Cerebral Artery Regions in Pediatric Moyamoya Disease: A Technical Note. *World Neurosurgery*, **118**, 324-328. https://doi.org/10.1016/j.wneu.2018.07.081

[14]   Hayashi, T., Shirane, R. and Tominaga, T. (2009) Additional Surgery for Postoperative Ischemic Symptoms in Patients with Moyamoya Disease: The Effectiveness of Occipital Artery-Posterior Cerebral Artery Bypass with an Indirect Procedure: Technical Case Report. *Neurosurgery*, **64**, E195-E196. https://doi.org/10.1227/01.NEU.0000336311.60660.26

[15]   Matsushima, Y. and Inaba, Y. (1984) Moyamoya Disease in Children and Its Surgical Treatment. Introduction of a New Surgical Procedure and Its Follow-Up Angiograms. *Childs Brain*, **11**, 155-170. https://doi.org/10.1159/000120172

[16]   Tu, Y.-K., Liu, H.-M., Kuo, M.-F., Wang, P.-J., *et al*. (1997) Combined Encephalo-Arterio-Synangiosis and Encephalo-Myo-Synangiosis in the Treatment of Moyamoya Disease. *Clinical Neurology and Neurosurgery*, **99**, S118-S22. https://doi.org/10.1016/S0303-8467(97)00070-X

[17]   Bang, J.S., Kwon, O.K., Kim, J.E., *et al*. (2012) Quantitative Angiographic Comparison with the Osiris Program between the Direct and Indirect Revascularization Modalities in Adult Moyamoya Disease. *Neurosurgery*, **70**, 625-633. https://doi.org/10.1227/NEU.0b013e3182333c47

[18]   Kawaguchi, T., Fujita, S., Hosoda, K., *et al*. (1996) Multiple Burr-Hole Operation for Adult Moyamoya Disease. *Journal of Neurosurgery*, **84**, 468-476. https://doi.org/10.3171/jns.1996.84.3.0468

[19]   Jeon, J.P., Kim, J.E., Cho, W.S., *et al*. (2018) Meta-Analysis of the Surgical Outcomes of Symptomatic Moyamoya Disease in Adults. *Journal of Neurosurgery*, **128**, 793-799. https://doi.org/10.3171/2016.11.JNS161688

[20]   Canavero, I., Vetrano, I., Zedde, M., *et al*. (2021) Clinical Management of Moyamoya Patients. *Journal of Clinical Medicine*, **10**, Article No. 3628. https://doi.org/10.3390/jcm10163628

[21]   Qian, Y., Huang, B., Hu, Z., *et al*. (2020) Analysis of Factors Related to Cerebral Infarction after Direct Bypass Surgery in Adults with Moyamoya Disease. *Cerebrovascular Diseases*, **49**, 55-61. https://doi.org/10.1159/000504743

[22]   Choi, S., Sung, J., Jo, E., *et al*. (2021) Language Treatment Effects on Communicative Abilities and Working Memory in Korean-Speaking Agrammatic Broca's Aphasia Caused by Moyamoya disease: Phase II Evidence from a Case Study. *Neurocase*, **27**, 297-307. https://doi.org/10.1080/13554794.2021.1950768

[23]   Shlobin, N., Frankel, H., Lam, S. (2021) Failures in Revascularization for Pediatric Moyamoya Disease and Syndrome: A Scoping Review. *World Neurosurgery*, **149**, 204-214.e1. https://doi.org/10.1016/j.wneu.2021.02.054

[24]   Case, D., Kumpe, D., Roark, C., *et al*. (2020) Neuroangiography: Review of Anatomy, Periprocedural Management, Technique, and Tips. *Seminars in Interventional Radiology*, **37**, 166-174. https://doi.org/10.1055/s-0040-1709171

[25]   Huguenard, A., Guerriero, R., Tomko, S., *et al*. (2021) Immediate Postoperative Electroencephalography Monitoring in Pediatric Moyamoya Disease and Syndrome. *Pediatric Neurology*, **118**, 40-45. https://doi.org/10.1016/j.pediatrneurol.2021.02.004

[26]   Kashiwazaki, D., Akioka, N., Kuwayama, N., *et al*. (2017) Berlin Grading System Can Stratify the Onset and Predict Perioperative Complications in Adult Moyamoya Disease. *Neurosurgery*, **81**, 986-991. https://doi.org/10.1093/neuros/nyx140

[27]   Uchino, H., Kuroda, S., Hirata, K., *et al*. (2012) Predictors and Clinical Features of Postoperative Hyperperfusion after

Surgical Revascularization for Moyamoya Disease: A Serial Single Photon Emission CT/Positron Emission Tomography Study. *Stroke*, **43**, 2610-2616. https://doi.org/10.1161/STROKEAHA.112.654723

[28] Yoon, H., Oh, H., Lee, H., *et al*. (2020) Effect of Sevoflurane Postconditioning on the Incidence of Symptomatic Cerebral Hyperperfusion after Revascularization Surgery in Adult Patients with Moyamoya Disease. *World Neurosurgery*, **134**, e991-e1000. https://doi.org/10.1016/j.wneu.2019.11.055

[29] Jo, W., Oh, H., Kim, H., *et al*. (2020) Preoperative Platelet Count May Predict Postoperative Symptomatic Cerebral Hyperperfusion Syndrome after Superficial Temporal Artery-Middle Cerebral Artery Anastomosis in Moyamoya Patients. *Clinical Neurology and Neurosurgery*, **199**, Article ID: 106260. https://doi.org/10.1016/j.clineuro.2020.106260

[30] Hayashi, T., Kimiwada, T., Karibe, H., *et al*. (2021) Preoperative Risks of Cerebral Infarction in Pediatric Moyamoya Disease. *Stroke*, **52**, 2302-2310. https://doi.org/10.1161/STROKEAHA.120.032699

[31] Roder, C., Haas, P., Fudali, M., *et al*. (2020) Neuropsychological Impairment in Adults with Moyamoya Angiopathy: Preoperative Assessment and Correlation to Mri and H_2 ^{15}O PET. *Neurosurgical Review*, **43**, 1615-1622. https://doi.org/10.1007/s10143-019-01192-3

[32] Agarwal, V., Singh, P., Ahuja, C., *et al*. (2021) Non-Invasive Assessment of Cerebral Microvascular Changes for Predicting Postoperative Cerebral Hyperperfusion after Surgical Revascularisation for Moyamoya Disease: An Arterial Spin Labelling MRI Study. *Neuroradiology*, **63**, 563-572. https://doi.org/10.1007/s00234-020-02583-w

[33] 翟明玉, 王勇, 吴丽敏, 杨佳, 韩明明, 黄祥, 李娟. 多模式监测对缺血型烟雾病血管重建术患者术后恢复的影响[J]. 临床麻醉学杂志, 2020, 36(7): 629-633.

[34] 孙彦熙, 步星耀, 袁强, 闫兆月, 马春晓, 屈鸣麒, 杨冬谊, 张慧. 联合血管重建术配合辛伐他汀治疗缺血型烟雾病的临床研究[J]. 中华脑科疾病与康复杂志, 2015, 5(1): 10-14.

[35] Kanamori, F., Araki, Y., Yokoyama, K., *et al*. (2021) Effects of Aspirin and Heparin Treatment on Perioperative Outcomes in Patients with Moyamoya Disease. *Acta Neurochirurgica*, **163**, 1485-1491. https://doi.org/10.1007/s00701-020-04668-0

[36] Liu, X., Zhang, D., Wang, S., *et al*. (2015) Clinical Features and Long-Term Outcomes of Moyamoya Disease: A Single-Center Experience with 528 Cases in China. *Journal of Neurosurgery*, **122**, 392-399. https://doi.org/10.3171/2014.10.JNS132369

[37] Huang, Z., Ding, X., Men, W., Zhang, D., *et al*. (2015) Clinical Features and Outcomes in 154 Patients with Haemorrhagic Moyamoya Disease: Comparison of Conservative Treatment and Surgical Revascularization. *Neurological Research*, **37**, 886-892. https://doi.org/10.1179/1743132815Y.0000000073