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慢性颈动脉粥样硬化闭塞治疗的研究进展

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[摘要] 慢性颈动脉粥样硬化闭塞会导致脑血流低灌注而增加卒中风险。无症状患者首选药物治疗, 对于反复出现神经症状的患者可选择手术治疗。颅外-颅内动脉旁路术(extracranial-intracranial artery bypass, EIAB)治疗效果不优于药物治疗。颈动脉内膜剥脱术(carotid endarterectomy, CEA)、颈动脉支架成形术(carotidartery stent, CAS)手术风险高、成功率低, 治疗效果尚待验证, 术前应严格筛选患者、把握适应证。本文就目前对于慢性颈动脉闭塞的治疗现状作一综述。

[关键词] 慢性颈动脉闭塞; 药物治疗; 手术治疗

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The treatment for chronic atherosclerotic occlusion of carotid: research progress

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[Abstract] Chronic atherosclerotic occlusion of carotid can lead to low cerebral blood flow and increase the risk of stroke. Drug therapy is the first choice for asymptomatic patients, while the patients with recurrent neurological symptoms may need surgical treatment. Extracranial-intracranial artery bypass (EIAB) is not better than medicine treatment. The operation risks of carotid endarterectomy (CEA) and carotidartery stent (CAS) are high with low success rate and the therapeutic effects remain to be verified. Therefore, the surgical indications should be strictly controlled. In this paper, the current status of treatment for chronic carotid artery occlusion was reviewed.

[Key Words] chronic carotid occlusion; medicine treatment; surgical treatment

慢性颈动脉闭塞年患病率约为 6/100 000, 由于部分患者因一过性症状未就诊, 实际患病率更高^[1]。动脉粥样硬化是引起颈动脉闭塞的主要原因, 病变好发于颈内动脉起始部。在药物治疗下, 闭塞侧的大脑半球年卒中率仍为 6%~20%^[1-2]。一侧颈动脉闭塞同时伴有对侧狭窄的患者, 其卒中或短暂性脑缺血发作(transient ischemic attack, TIA)发生率更高, 每年约为 10%^[3]。慢性颈动脉闭塞患者的卒中症状主要是由脑血流低灌注导致。改善脑血流灌注可以缓解神经症状, 降低卒中发生率和死亡率, 但治疗方式的选择目前仍有争议。

1 药物治疗

目前关于慢性颈动脉闭塞药物治疗的经验较少, 主要还是基于颈动脉狭窄和卒中的二级预防, 实施抗血小板及他汀类药物治疗方案。高血压病、

高脂血症、糖尿病和吸烟等是颈动脉闭塞患者再发卒中的主要危险因素, 应积极控制。对于症状性颈动脉闭塞患者, 尤其当临床特征(如肢体抖动样发作、直立性 TIA、慢性眼部缺血综合征)和辅助检查表明是由血流动力学异常引起的症状时, 要避免快速降压, 以免诱发脑缺血^[4]。他汀类药物能有效降低卒中风险, 约为 5%^[5]。有研究^[6]推荐将低密度脂蛋白降低到 1 000 mg/L。此外, 调整生活方式如戒烟限酒、适当运动也可降低卒中发生率。Markus 等^[7]研究发现, 对于近期出现症状的颈动脉狭窄患者, 氯吡格雷联合阿司匹林(双抗联合治疗)比单独服用阿司匹林更能有效减少无症状栓塞事件。对于有明确指征, 如症状性颅内动脉狭窄、TIA、小卒中患者, 双抗联合治疗 3 个月能够有效预防卒中^[8-9]。但在远期结局(>2 年)包括心肌梗死、心血管因素引起的卒中、死亡事件的发生率上, 两者区

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别不大^[10],双抗联合还会增加出血风险^[11]。因此,颈动脉闭塞患者建议卒中后 3 个月内双抗联合治疗,之后可削减为单用阿司匹林或氯吡格雷,以减少出血风险。约 2.3% 颈动脉闭塞患者可以自发远期再通^[12],这可能是由原病变部位纤维蛋白溶解^[12]或滋养血管建立了侧支循环^[13]所致。有研究^[14]认为,同侧缺血事件发生超过 6 个月可认为无症状,但是否应以无症状性颈动脉狭窄来治疗自发再通患者,目前尚没有定论。

2 手术治疗

2.1 颅外-颅内动脉旁路术 (extracranial-intracranial artery bypass, EIAB) 2014 年美国心脏病学会基金会 (ACCF) 和美国心脏协会 (AHA) 指南^[6]指出,对于近 6 个月内发生 TIA 或缺血性卒中伴有大脑中动脉或颈动脉狭窄或闭塞的患者,不建议进行 EIAB (A 类证据)。1985 年,大型、前瞻性、多中心的颅外-颅内 (extracranial-intracranial, EC/IC) 旁路试验 (1 377 例)^[15]纳入标准为: (1) 患者既往 TIA 或小卒中病史; (2) 大脑中动脉 (MCA) 主干或主要分支的狭窄或闭塞, C₂ 椎体以上的颈动脉闭塞 (无法行颈动脉内膜剥脱术)。研究^[15]显示: 对于颈动脉闭塞患者卒中的远期 (5 年) 预防效果, EC/IC 手术组和药物组分别为 31%、29%, 但差异无统计学意义。然后日本 EC/IC 旁路试验 (Japanese EC/IC bypass trial, JET) 和北美颈动脉调查 (carotid occlusion surgery study, COSS) 通过脑流动力学标准纳入高风险患者进行研究^[16-18]。JET 试验 2 次中期分析共纳入 196 例患者, 结果显示, 药物组和手术组到达临床终点分别为 14/98 和 5/98 (Kaplan-Meier 分析, $P=0.046$), 但没有提及围手术期卒中发生率和死亡率, 且试验完成后至今未公布最终结果。COSS 研究最终纳入 195 例患者, 主要终点事件定义为 30 d 内卒中或死亡, 以及 2 年内发生同侧缺血性卒中。研究结果显示: 30 d 内闭塞同侧卒中发生率约为 14.4%; 2 年的随访结果显示手术组与药物组卒中风险相近 (22.7% vs 21.0%, $P=0.78$)。由此可见, EC/IC 旁路术治疗颈动脉闭塞与药物治疗相比不具优势。

2.2 颈动脉内膜剥脱术 (carotid endarterectomy, CEA) CEA 作为治疗颈动脉粥样硬化性狭窄、预防缺血性卒中较为有效, 然而对症状性颈动脉闭塞的 CEA 治疗目前仍有争议。对于节段性闭塞颈动

脉的治疗, CEA 或联合 Fogarty 导管取栓术仍然是一种安全有效的方法^[19]。对于一侧闭塞伴对侧狭窄的治疗, CEA 可以改善双侧脑血流, 降低颈动脉闭塞后的卒中发生率^[20], 但重建闭塞血管血运的成功率低, 为 34%~83%^[21-22], 且围手术期风险较高^[23]。术前的充分评估和严格的手术适应证是颈动脉闭塞 CEA 再通成功的关键, 主要包括: (1) 颈内动脉局限性闭塞, 远端可见反流血; 如远端有新鲜血栓形成, 则可联合 Fogarty 导管取栓^[19]; 但慢性颈动脉闭塞病变由于形成时间过长, 颈动脉闭塞处斑块及血栓逐渐机化、纤维化、钙化, 颈动脉变细, 不能彻底切除动脉粥样硬化斑块的内膜, 因而降低手术成功率^[24]。(2) MRI 观察既往脑梗死的大小和范围以及有无新鲜梗死, 尽量避免在脑梗死急性期进行 CEA, 从而降低缺血再灌注损伤甚至脑出血概率。研究^[19-26]表明, 颈动脉闭塞症状出现后 2 周内施行 CEA 是安全有效的治疗方法之一。

2.3 颈外动脉内膜剥脱术 (external carotid artery endarterectomy, ECAR) 当颈内动脉广泛闭塞不能行 CEA, 或 CEA 联合 Fogarty 导管取栓术仍无反流血或反流血仍不满意时, 且同时伴颈外动脉 (external carotid artery, ECA) 疾病时, 可通过 ECAR 增加侧支循环血流以延长无卒中生存期^[21-27]。在 Gertler 等^[27]的研究中, 195 例患者术后 30 d 内神经并发症发生率为 5%, 死亡率为 3%。但这项研究中, 许多患者曾先行颈内、外动脉旁路术或颈动脉-锁骨下动脉旁路术, 这可能增高 ECAR 的术后风险。1 年后, 1 项纳入 192 例患者仅针对 ECAR 的研究^[28]显示, 围手术期的神经并发症发生率为 1.6%, 死亡率为 0。近期的一项研究^[29]纳入了 27 例患者, 术后围手术期的神经并发症发生率为 13.7%, 死亡率为 0, 3 年内卒中发生、死亡累计率为 17%, 颈外动脉通畅率为 80%。尽管 ECAR 开展已有 50 年, 但其确切适应证仍然不明, 结果也缺乏大型随机对照试验验证。在无症状或出现严重卒中颈动脉闭塞患者中, ECA 血运重建似乎没有作用^[30]。双侧颈动脉闭塞患者行 ECAR 可增加脑血流灌注, 减轻症状, 且手术风险低^[25]。

2.4 颈动脉支架成形术 (carotid artery stent, CAS) 早先认为颈动脉闭塞无法运用支架成形术治疗, 主要原因是导丝无法通过闭塞部位。随着技术、材料的进步, 颈动脉闭塞腔内治疗成为可能。颈动脉闭塞患者腔内治疗的标准没有明确, 其适应

证主要基于经验总结^[31-38],包括:(1)经药物治疗无效,患侧症状反复发作;(2)术前评估(CT 灌注、MR 灌注、PET-CT、SPECT-CT 等)确定患侧脑半球低灌注;(3)同侧颈外动脉、眼动脉向颅内供血,同时有血液反流至海绵窦段以下;(4)闭塞近端有残端;(5)患者一般情况较好,无明显神经功能障碍或大面积脑梗死。Lin 等^[34]研究显示,54 例患者中,手术成功率为 65%(35/54)。3 个月内卒中和死亡占 4%,短期并发症发生率、死亡率均较低。但是该研究并没有提供具体技术细节。理论上,颈动脉闭塞段在闭塞前存在一道“真腔”,微导丝探及此潜在的“真腔”是该手术的关键。但手术难点之一是无法通过路图模式观察导丝通过该“真腔”的过程。有病例报道^[38]发现,闭塞段前侧壁通过的成功率较高,这可能与动脉粥样斑块好发于颈内动脉分叉后壁并逐渐增厚向前壁发展有关^[39]。需要注意的是,在通过闭塞段后,导丝在经过颈内动脉岩部时可能存在一处极度弯曲的血管,这里也是手术操作导致夹层或穿孔的好发部位^[38]。另外还应考虑高灌注损伤和远端栓塞。再灌注损伤在脑血流储备不足的患者中更容易发生^[40]。控制血压在预防高灌注综合征上非常重要。远端脑保护装置可有效预防远端栓塞,对于远端难以放置的,可先使用近端脑保护装置,在导丝通过闭塞段后,再放置远端脑保护装置^[41]。

3 展 望

症状性颈动脉闭塞发病率低,未来仍需要前瞻性、多中心的随机对照试验来比较并证实药物、开放手术、介入技术的治疗效果。虽然当前 ACCF/AHA 指南不建议对闭塞的颈动脉进行血运重建,但对于特定的患者,血运重建带来的益处仍将高于风险,对于这类患者的筛选仍缺乏严格的标准。此外,尽管血管腔内技术治疗颈动脉闭塞取得了长足的进步,但其有效性与安全性还需要大型随机对照试验进一步验证。

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