

心脑血管疾病的“脑心同治”

施铭岗 佟小光

【摘要】 动脉粥样硬化是脑血管病和心血管病共同的病理生理学机制,二者为同源性疾病,可共病,这也是“脑心同治”的病理生理学基础。近年随着药物治疗和手术技术改进,“脑心同治”得以实现并提高临床疗效。本文综述“脑心同治”策略,以为心脑血管疾病的治疗提供理论基础和临床指导。

【关键词】 脑血管障碍; 心血管疾病; 神经外科手术; 心血管外科手术; 综述

Synchronous surgical treatment for brain and heart of cardiovascular and cerebrovascular diseases

SHI Ming-gang, TONG Xiao-guang

Hybrid Cerebrovascular Surgery Ward, Department of Neurosurgery; Laboratory of Microneurosurgery, Tianjin Neurosurgical Institute; Clinical College of Neurology, Neurosurgery and Neurorehabilitation, Tianjin Medical University; Tianjin Key Laboratory of Cerebrovascular and Neural Degenerative Diseases; Tianjin Key Laboratory of Cerebral Revascularization and Head and Neck Neuro - Oncology for Technology Transformation, Tianjin Huanhu Hospital (Tianjin Central Hospital for Neurosurgery and Neurology), Tianjin 300350, China

Corresponding author: TONG Xiao-guang (Email: Tong_xg@139.com)

【Abstract】 Cardiovascular and cerebrovascular diseases are homologous diseases and can be comorbidities. Atherosclerosis is the pathological basis of the comorbidities of cardiovascular and cerebrovascular diseases. In recent years, with the improvement of surgical technique and the progress of drug intervention, the synchronous surgical treatment for brain and heart of cardiovascular and cerebrovascular diseases can improve clinical outcome. This article reviews the synchronous surgical treatment for brain and heart of cardiovascular and cerebrovascular diseases, in order to provide theoretical basis and clinical guidance for the cardiovascular and cerebrovascular diseases.

【Key words】 Cerebrovascular disorders; Cardiovascular diseases; Neurosurgical procedures; Cardiovascular surgical procedures; Review

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心脑血管疾病是人类病残、病死的重要原因,其病死率居全球死亡原因的首位^[1]。脑血管病和心血管病为同源性疾病,二者可共病,这也是“脑心同治”的病理生理学基础。“脑心同治”包含两种含义,一是同时外科干预,二是同种治疗方法。本文拟综述“脑心同治”策略,以为心脑血管疾病的治疗提供理论基础和临床指导。

一、心脑血管疾病发病机制

动脉粥样硬化是脑血管病和心血管病共病的病理生理学基础,属全身性疾病,由于累及部位和发病顺序不同而表现出不同临床症状。动脉粥样硬化是一种慢性炎症性改变,在血流动力学作用下于大动脉和中动脉内产生低剪应力区,该区域常是粥样硬化斑块产生区,随着斑块形成,含有脂蛋白的载脂蛋白B(ApoB)进入血管内皮下间隙,被天然免疫细胞识别为危险信号并加以修饰,激活Toll样受体(TLR)和炎性小体,产生和释放炎症因子,促进单核细胞向斑块募集,引起炎症反应。单核细胞通过分化增殖或血管平滑肌细胞横向分化为巨噬细胞,然后摄取斑块内脂蛋白形成泡沫细胞,这是斑块形成坏死核心的基础,单核细胞持续聚集、脂蛋

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作者单位:300350 天津市环湖医院(天津市脑系科中心医院) 神经外科复合脑血管外科病区 天津市神经外科研究所显微神经外科实验室 天津医科大学神经内外科及神经康复临床学院 天津市脑血管与神经变性重点实验室 天津市脑血流重建与头颈神经肿瘤新技术转化重点实验室

通讯作者:佟小光,Email:Tong_xg@139.com

白摄取增加可导致斑块负荷加重。包含巨噬细胞、树突状细胞和 B 淋巴细胞在内的抗原呈递细胞 (APC) 将脂抗原和肽抗原分别提呈给恒定自然杀伤 T 细胞 (iNKT) 和 T 淋巴细胞, 后者参与获得性 T 淋巴细胞和 B 淋巴细胞免疫反应, 这一过程可造成血管内皮细胞功能障碍, 进一步加剧炎症反应。针对上述炎症反应过程的节点进行控制, 有望成为心脑血管疾病的重要治疗方法^[2-3]。

二、心血管病治疗过程中并发的脑血管病

缺血性卒中是冠状动脉旁路移植术 (CABG) 的主要并发症, 其发生率约为 1.3%, 女性、高龄、术前伴发神经系统症状、重度颈动脉狭窄、主动脉弓钙化、充血性心力衰竭、合并糖尿病、既往有脑卒中病史等为其主要危险因素^[4-5]。体外循环手术后并发脑卒中的概率为 0.5%~7%, 冠状动脉旁路移植术为 3.8%, 非体外循环下冠状动脉旁路移植术为 1.9%, 主动脉瓣手术为 4.8%, 二尖瓣手术为 8.8%, 双瓣或三瓣手术为 9.7%, 冠状动脉旁路移植术联合心脏瓣膜手术为 7.4%, 且体外循环时间延长是术后并发脑卒中的重要危险因素; 冠状动脉旁路移植术后并发神经系统并发症的患者病死率高达 24.8%, 且住院时间明显延长^[6]。心脏手术后并发缺血性卒中的作用机制主要为心脏手术导致血流动力学改变、体外循环导致血流动力学不稳、主动脉弓部操作导致栓子脱落或气栓堵塞脑血管、脑低灌注等, 其危险因素包括年龄 > 60 岁, 颈动脉狭窄程度 > 50%, 既往有缺血性卒中或短暂性脑缺血发作 (TIA)、充血性心力衰竭、心脏瓣膜病、心肌梗死病史, 二次心脏手术, 术后房颤, 术中冠状动脉旁路移植时间 > 2 小时等^[5-6]。尽管心脏手术围手术期并发脑卒中的机制不同, 但多认为与颈内动脉狭窄程度相关^[6]。

三、脑血管病治疗过程中并发的心血管病

颈动脉狭窄与冠心病密切相关, 脑卒中患者并发冠心病的概率为 18%~38%, 接受颈动脉内膜切除术 (CEA) 的患者为 35%~49.1%, 接受颈动脉支架成形术 (CAS) 的患者则高达 77.1%^[7]。颈动脉内膜切除术和颈动脉支架成形术后心肌梗死最为常见, CREST (Carotid Revascularization Endarterectomy versus Stenting Trial) 显示, 颈动脉内膜切除术后心肌梗死发生率约为 2.25%, 颈动脉支架成形术后则降至 1.13%^[8]; 且行颈动脉支架成形术的患者无论是否伴发神经系统缺血症状, 术后心肌梗死发生率并无明显差异, 而术后出现心肌梗死或血清心肌酶

谱水平升高则提示死亡风险增加^[7]。颈动脉内膜切除术术后心肌梗死风险更高的原因可能为, 颈动脉支架成形术前常规行双联抗血小板治疗, 间接降低术后心肌梗死风险; 颈动脉内膜切除术多采取全身麻醉, 术中可能诱发心律失常和血压波动, 增加心肌梗死风险, 加之颈部切口可能诱发局部炎症反应, 释放炎症因子, 导致心肌梗死。颈动脉内膜切除术和颈动脉支架成形术后并发心肌梗死的机制尚不明确, 多认为脑血管手术导致血流动力学改变是重要诱因, 且高龄、既往有冠心病病史、周围血管病变、血管再狭窄等均为颈动脉内膜切除术后发生心肌梗死的危险因素。研究显示, 颈动脉、下肢动脉等非心血管手术围手术期心肌梗死风险与全身性动脉粥样硬化有关, 且围手术期心肌梗死发生率与病死率相关, 心脑血管疾病患者围手术期心肌梗死病死率是轻型脑卒中患者的 5 倍^[9], 因此颈动脉内膜切除术和颈动脉支架成形术后应常规评估心肌梗死风险。未来颈动脉内膜切除术和颈动脉支架成形术的重点应是降低术后脑卒中和围手术期心肌梗死发生率, 以提高手术安全性^[10]。

四、心脑血管疾病的治疗

Illuminati 等^[11]纳入 426 例无冠心病病史且心脏超声和心电图均正常的拟行颈动脉内膜切除术患者, 随机予颈动脉内膜切除术并术前常规冠状动脉筛查 (A 组, 216 例) 和单纯颈动脉内膜切除术 (B 组, 210 例), 术前常规筛查冠状动脉的患者中 30.56% (66/216) 合并冠心病并行经皮冠状动脉介入术 (PCI), 此类患者术后均未发生心肌梗死, 而单纯行颈动脉内膜切除术的患者术后心肌梗死发生率为 2.86% (6/210); 随访 6 年, 颈动脉内膜切除术并术前常规冠状动脉筛查的患者心肌梗死发生率为 1.39% (3/216), 而单纯行颈动脉内膜切除术的患者为 15.71% (33/210), 提示脑血管病治疗过程中发现心血管病高危患者并及时干预, 可降低心血管并发症的发生风险。冠状动脉旁路移植术围手术期脑卒中发生率约为 5.2%, 与脑血管狭窄程度相关^[12-13]。采取颈动脉内膜切除术联合冠状动脉旁路移植术同期手术的患者术后心肌梗死和脑卒中发生率均明显低于分期手术; 分期手术若先行颈动脉内膜切除术, 术后心肌梗死发生率增加, 若先行冠状动脉旁路移植术, 术后神经系统并发症发生率增加^[14-15]; “脑心同治”则可在围手术期为心脏和脑同时提供保护, 避免发生缺血性损害。颈动脉内膜切除术联

合冠状动脉旁路移植术同期手术由 Bernhard 等^[16]于 1972 年率先开展,可有效降低病死率以及术后短期和远期脑卒中复发率,缩短住院时间。研究显示,颈动脉支架成形术联合冠状动脉旁路移植术同期手术后脑卒中发生率是颈动脉内膜切除术联合冠状动脉旁路移植术同期手术的 2 倍,提示颈动脉内膜切除术的疗效可能优于颈动脉支架成形术,尤其对于近期脑卒中患者^[17]。亦有研究得出相反结论,颈动脉内膜切除术联合冠状动脉旁路移植术同期手术风险高于分期手术,不稳定型心绞痛或既往有脑卒中或短暂性脑缺血发作病史的患者通常倾向颈动脉内膜切除术联合冠状动脉旁路移植术同期手术,而无神经系统症状的稳定型心绞痛患者通常采取颈动脉内膜切除术联合冠状动脉旁路移植术分期手术^[18]。该项研究还显示,颈动脉支架成形术联合冠状动脉旁路移植术的疗效优于颈动脉内膜切除术联合冠状动脉旁路移植术^[18],但颈动脉支架成形术后远期脑卒中复发率高于颈动脉内膜切除术^[19],因此认为,对于存在颈动脉内膜切除术高风险的患者选择颈动脉支架成形术有助于减少围手术期并发症风险。对于伴发无症状重度颈内动脉狭窄的冠心病患者,若脑卒中风险较低,则行冠状动脉旁路移植术的同时对颈内动脉保守处理;若存在神经系统症状,则优先考虑冠状动脉旁路移植术前或同时行颈内动脉支架成形术,以避免颈动脉内膜切除术增加心肌梗死风险^[4]。尽管颈动脉内膜切除术联合冠状动脉旁路移植术同期手术的并发症风险较高,但单纯行冠状动脉旁路移植术的脑卒中并发症风险亦较高^[20],尚待探究更合理的干预策略以提高远期疗效,降低术后病残率和病死率。有学者在颈动脉内膜切除术与冠状动脉旁路移植术之间采取麻醉唤醒,可尽早发现颈动脉内膜切除术后脑卒中风险、及时纠正神经功能障碍,避免冠状动脉旁路移植术加重脑卒中进展^[21]。有学者推荐,对于脑血管病风险较高如伴发神经系统症状、双侧颈内动脉重度狭窄(狭窄率 > 80%)、单侧或双侧颈总动脉闭塞、单侧颈总动脉中至重度狭窄伴对侧闭塞、无症状颈总动脉重度狭窄(狭窄率 > 80%)伴脑低灌注的冠心病患者,可采取颈动脉内膜切除术和冠状动脉旁路移植术分期手术,通常间隔 6.87 ~ 32.4 天,分期手术期间心肌梗死发生率为 2.5% ~ 24%,且手术间隔时间越短、心脏并发症越少^[22]。亦有学者以颈动脉支架成形术替代颈动脉内膜切

除术对伴颈动脉狭窄的冠心病患者行分期手术,术后心肌梗死发生率和病死率均降低,而脑卒中风险增加^[23],但 1 年后的随访结果更支持颈动脉支架成形术联合冠状动脉旁路移植术分期手术^[24]。颈动脉支架成形术联合冠状动脉旁路移植术同期手术后发生心肌梗死、脑卒中和死亡的总概率为 2.2% ~ 4.5%^[6],但该项研究所纳入的主要为无症状颈内动脉狭窄患者。研究显示,伴发脑缺血症状的冠心病患者颈动脉支架成形术联合冠状动脉旁路移植术同期手术后脑卒中发生率是颈动脉内膜切除术联合冠状动脉旁路移植术同期手术患者的 5 倍,而不伴脑缺血症状的患者术后脑卒中发生率和病死率低于颈动脉内膜切除术联合冠状动脉旁路移植术同期手术患者,因此,对于不宜行颈动脉内膜切除术的患者可采用颈动脉支架成形术联合冠状动脉旁路移植术同期手术^[25]。Meta 分析显示,颈动脉支架成形术联合冠状动脉旁路移植术同期手术与分期手术后并发症发生率无明显差异,但术前伴发神经系统症状的患者术后并发症发生率更高^[17]。约 80% 行颈动脉支架成形术联合冠状动脉旁路移植术同期手术的患者为无症状单侧颈内动脉重度狭窄患者,术后 30 天脑卒中发生率和病死率为 6.7%,发生脑卒中、心肌梗死和死亡的总体概率为 8.5%;而有脑卒中或短暂性脑缺血发作病史的患者脑卒中发生率高达 15%,发生脑卒中和死亡的概率为 10% ~ 23%^[17]。目前,颈动脉内膜切除术联合冠状动脉旁路移植术同期还是分期手术尚存争议,支持分期手术者认为,同期手术并发症如围手术期脑卒中发生率和病死率较高;支持同期手术者未发现同期与分期手术围手术期脑卒中发病率和病死率存在明显差异,考虑与心脑血管狭窄程度和血管代偿有关,且多系统动脉粥样硬化导致预后较差并非为手术所致,因此认为颈动脉内膜切除术联合冠状动脉旁路移植术同期与分期手术后病死率、脑卒中和心肌梗死发生率无明显差异^[26]。但这两种治疗方案尚缺乏大样本随机对照临床试验,因此美国心脏协会(AHA)/美国心脏病学会(ACC)均予以推荐。

随着血管内介入技术的发展,心脑血管疾病的治疗有了更多选择。颈内动脉起始部狭窄行支架成形术后脑卒中发生率和病死率高于内膜切除术,但心肌梗死发生率低于内膜切除术^[27]。2019 年的一项研究显示,颈动脉内膜切除术联合冠状动脉旁路移植术同期手术围手术期并发症约 6.8%^[28],低于

既往文献报道的 9%~12%^[29],其差异可能部分归因于药物干预和手术技术进步,但更主要取决于疾病特征及并发症等因素,如围手术期并发症发生率较高的患者术前可能存在脑缺血。与症状性或双侧颈内动脉狭窄相比,单侧颈内动脉狭窄患者术后脑卒中发生率和总体并发症发生率均较低^[30],表明病例选择对减少围手术期并发症具有重要意义。心脑血管解剖学特征及临床特征亦影响术后疗效,如对侧动脉闭塞、动脉多发狭窄,颈内动脉高颈段狭窄、颈动脉内膜切除术后再次狭窄、行双侧颈动脉支架成形术、既往有颈部放疗史或颈部分离手术史、颈椎不稳定,以及其他高风险因素如年龄 > 75 岁、冠状动脉多支病变、合并心绞痛、充血性心力衰竭、左心室射血分数 < 30%、近期发生心肌梗死(≤ 72 小时至 6 周)、严重慢性阻塞性肺病(COPD)、永久性对侧脑神经损伤、慢性肾功能障碍等均可增加手术风险^[31]。有学者提出,颈动脉内膜切除术联合非体外循环下冠状动脉旁路移植术(OPCABG)后 30 天发生脑卒中和死亡的概率以及发生脑卒中、心肌梗死和死亡的概率与颈动脉支架成形术联合冠状动脉旁路移植术相当^[6]。颈动脉内膜切除术联合非体外循环下冠状动脉旁路移植术同期手术后发生脑卒中和死亡的概率最低(2.2%),究其原因:体外循环可以导致血压下降,特别是存在颈内动脉狭窄或溃疡斑块时,可显著增加围手术期脑卒中风险。体外循环下冠状动脉旁路移植术需严格抗凝,增加术后颅内出血的潜在风险。行颈动脉支架成形术联合冠状动脉旁路移植术同期手术前需服用阿司匹林 100 mg/d(至少 2~5 d)或手术当日服用阿司匹林负荷量(300 mg),先行颈动脉支架成形术时还需静脉肝素化(100 U/kg)以维持活化凝血时间(ACT) ≥ 250 ms,再行冠状动脉旁路移植术时维持活化凝血时间 > 450 ms,术毕静脉滴注鱼精蛋白中和肝素,术后 6 小时无明显出血予氯吡格雷负荷量(300 mg),并维持双联抗血小板治疗至少 1 个月^[32-33]。

总之,心脑血管疾病是人类主要死因之一,动脉粥样硬化是其共同病因,炎症反应是重要病理生理学基础,目前的“脑心同治”主要包括药物治疗和外科手术,后者主要为颈动脉支架成形术或颈动脉内膜切除术联合冠状动脉旁路移植术同期或分期手术,随着病理生理学机制的深入研究以及手术技术的改进,“脑心同治”必将获得更好的临床疗效。

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下期内容预告 本刊2024年第2期报道专题为“脑心共病”,重点内容包括:树立“脑心同治”观念 助力“脑心共病”诊断与治疗发展;慢性心力衰竭与中枢神经系统相互作用对“脑心同治”理念的启示;心脏与脑之间关联性及其机制研究;地中海饮食与健康老龄化研究;动脉粥样硬化性缺血性卒中合并冠心病研究;脑卒中后房颤机制及治疗;心脏MRI对脑卒中相关隐匿性心源性栓塞的诊断价值;经颅多普勒超声监测在心脏大血管手术中的应用;非瓣膜性房颤合并缺血性卒中抗凝治疗启动时机;感染性心内膜炎抗凝治疗相关脑血管并发症治疗策略;主动脉夹层脑部并发症危险因素及治疗策略