·泛血管医学时代"脑心同治"手术·

主动脉弓部手术围手术期的脑保护

唐一鹏 白云鹏 陈庆良

【摘要】 体外循环和停循环下维持最佳脑灌注是主动脉弓部手术中脑保护的基础。脑保护策略包括低温、脑灌注、药物治疗和血气管理,已应用于临床,但最佳策略仍难确定。主动脉弓部手术中脑保护的临床结局在很大程度上取决于脑温、停循环时间和脑灌注类型,最佳的脑保护策略应是在全面脑监测的基础上进行个体化治疗,有效减少脑损伤。本文总结体外循环下主动脉弓部手术脑监测与管理方法或指标以及围手术期脑保护策略,以指导主动脉弓部手术中脑保护的临床实践。

【关键词】 主动脉,胸; 体外循环; 心血管外科手术; 围手术期; 综述

Brain protection in perioperative period of aortic arch surgery

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【Abstract】 Maintaining optimal cerebral perfusion during cardiopulmonary bypass and circulatory arrest is basis of intraoperative management of aortic arch surgery. Various cerebral protection techniques including hypothermia, cerebral perfusion, drug protection and blood gas management have been used in the clinic, but the optimal strategy remains difficult to determine. The clinical outcome of cerebral protection in aortic arch surgery largely depends on brain temperature, circulatory arrest time and cerebral perfusion at the time of circulatory arrest. The optimal brain protection strategy should be individualized treatment on the basis of comprehensive brain monitoring, so as to effectively reduce the occurrence of brain injury. This article summarizes the means or indicators of brain monitoring and management during cardiopulmonary bypass in aortic arch surgery, as well as perioperative brain protection strategies, in order to guide the clinical practice of intraoperative brain protection in aortic arch surgery.

【Key words】 Aorta, thoracic; Extracorporeal circulation; Cardiovascular surgical procedures; Perioperative period; Review

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主动脉弓部手术指手术治疗主动脉瘤或主动脉夹层过程中部分或完全替换主动脉弓的外科手术,随着手术技术的发展,其临床结局有所改善,但病死率及神经系统并发症发生率仍较高[1-2]。主动脉弓部手术围手术期神经系统并发症分为永久性和短暂性神经功能障碍[3],发生率分别为7.3%~12.8%和8.0%~10.3%[4],其中永久性神经功能障碍如脑卒中的主要原因是术中主动脉及其分支栓子脱落导致脑栓塞;短暂性神经功能障碍如谵妄、肢体麻木、失语等较脑卒中更常见,但发生机制尚不明确。有效的脑保护是保证主动脉弓部手术预后良好的重要措施,通过体外循环避免脑缺血或脑低灌注是目前脑保护的重点。本文拟总结体外循环下主动脉弓部手术脑监测和管理方法或指标,构建脑保护策略框架及相关临床问题,以期指导主动脉弓部手术中脑保护的临床实践,减少术后神经系统

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并发症。

一、体外循环下主动脉弓部手术脑监测与管理方法或指标

1.经食管超声心动图　经食管超声心动图(TEE)可用于检测升主动脉粥样硬化斑块,辅助心血管外科医师确定主动脉钳夹和插管位置,避免斑块脱落造成脑栓塞;同时还可在体外循环结束前识别心腔残留气体并指导术者将气体完全排出,避免体内气栓流动造成脑缺血。

2.平均动脉压　主动脉弓部手术体外循环过程中脑损伤尤其是短暂性神经功能障碍,主要是由于术中脑低灌注所致,而体外循环过程中最佳平均动脉压(MAP)一直存有争议。一项大样本回顾性研究显示,体外循环下平均动脉压降低(< 64 mm Hg,持续 > 10 min)与术后脑卒中发生率增加密切相关,且术中避免低血压可减少术后脑卒中风险[5]。而一项随机对照临床试验结果显示,与体外循环下40 ~ 50 mm Hg的平均动脉压相比,70 ~ 80 mm Hg的平均动脉压无法降低术后缺血性卒中发生率和严重程度[6]。最新证据表明,最佳平均动脉压应在脑血流自动调节范围内(50 ~ 130 mm Hg)[7-8]。平均动脉压低于脑血流自动调节下限,可导致脑卒中发生率和病死率增加;平均动脉压超过脑血流自动调节上限,则与谵妄发生率增加有关[8-10],故体外循环下保持平均动脉压高于脑血流自动调节下限可以降低术后谵妄发生率[11]。目前尚无针对主动脉弓部手术中维持灌注的最佳平均动脉压的随机对照试验。笔者认为,除停循环下实施脑保护策略外,主动脉弓部手术中维持平均动脉压于脑血流自动调节范围亦是减少脑损伤的重要手段。目前停循环下脑灌注流量多为10 ml/(kg·min)[12],然而随着体温的下降,脑代谢也相应降低,故笔者认为这一脑灌注流量相对较高,可将低温(24 ~ 28 ℃)停循环下顺行脑灌注流量控制在6 ~ 7 ml/(kg·min),术后脑缺血并发症发生率无明显升高。

3.脑温监测　由于脑代谢旺盛,主动脉弓部手术中准确测量脑温对脑保护至关重要。脑温直接测量不切实际,可采取替代位点[13]。颈静脉球温度可较敏感地反映低温期间脑实质温度,但需颈静脉穿刺置入测温探头,为侵入性操作,故未被临床采用[14]。美国胸外科医师学会(STS)、美国心血管麻醉医师协会(SCA)及美国体外循环技术学会(AmSECT)联合发布的《体外循环临床实践指南》[15]建议,通过鼻咽温度或肺动脉温度监测脑温(Ⅱa类推荐),或采用体外循环下动脉出口或脑灌注血液温度代表体外循环下脑温(Ⅰc类推荐)[15]。此外,低温快速复温可导致严重脑损伤[16],复温期间应避免脑温 > 37 ℃,氧合器显示的动脉出口与静脉流入之间温度梯度 ≤ 10 ℃[15]。

4.脑电监测　低温下行主动脉弓部手术可降低脑电活动和脑代谢,脑电静默被认为是脑代谢需求降至最低的标志物[17],故将脑温冷却至脑电静默状态是停循环下脑保护的措施之一。但脑电图仅可监测大脑皮质浅层缺血,而无法监测皮质下、脑深部区域缺血;此外,既往脑缺血病史、应用麻醉药、体温过低、体外循环和电烧灼等因素均可影响脑电图检测脑缺血的敏感性[18],因此脑电图变化无法预测术后脑缺血和脑卒中的发生。脑电双频指数(BIS)是应用非线性相位锁定原理对原始脑电图波形进行处理并量化的持续脑电监测技术[19],临床较为常用,但心脏手术中脑电双频指数与患者术中意识和麻醉深度、术后谵妄和神经系统并发症之间的相关性仍存争议[18],目前尚无探究脑电双频指数影响主动脉弓部手术低温停循环下脑功能的前瞻性研究,有待进一步探索主动脉弓部手术中脑电监测手段。

5.经颅多普勒超声　经颅多普勒超声(TCD)主要用于大脑中动脉等颅内大动脉的血流检测,是主动脉弓部手术中检测微栓子和大栓子的敏感手段,可测量脑血流量及其分布,有助于优化停循环下顺行脑灌注策略。对于Willis环不完整的患者,TCD检测到交叉灌注不充分提示可以从单侧脑灌注转换为双侧脑灌注。

6.近红外光谱　近红外光谱(NIRS)通过测量600 ~ 900 nm处饱和和不饱和血红蛋白的吸收特性以确定局部脑氧饱和度。主动脉弓部手术中局部脑氧饱和度麻醉后即刻(基线) < 50%或较基线下降 > 20%,提示脑缺血或脑低灌注[20]。有研究认为,局部脑氧饱和度对术后脑卒中和认知功能障碍的预测价值较小,但多为回顾性研究或小型前瞻性研究[21],参考价值有限。一项纳入7项随机对照试验计1138例接受心脏手术患者的系统综述显示,近红外光谱测量局部脑氧饱和度与预测术后脑卒中之间无关联性[22]。另一项队列研究通过近红外光谱检测到大脑交叉灌注中断,提示临床医师将单侧脑灌注转换为双侧顺行脑灌注,转换后局部脑氧饱和

度恢复正常[23]。该技术亦有其局限性:(1)近红外光谱主要监测大脑前动脉和大脑中动脉灌注区,且仅识别最大深度为3 ~ 4 cm的脑组织信号[24]。(2)近红外光谱监测局部脑氧饱和度的算法需假设动脉与静脉之间血容量分布固定(动脉占25% ~ 30%、静脉占70% ~ 75%),而动脉与静脉血容量分布的个体间差异可影响主动脉弓部手术不同阶段局部脑氧饱和度的准确性。(3)近红外光谱测量局部脑氧饱和度可监测局部脑皮质氧气输送与消耗的平衡,受血氧含量、脑代谢率和脑血流量等因素的影响,此外,体外循环、监测部位温度、血液稀释、动脉血氧分压和二氧化碳分压等亦可影响近红外光谱测量的准确性[24-25]。

7.频域近红外光谱和漫反射光谱 频域近红外光谱(FD-NIRS)和漫反射光谱是较近红外光谱更先进的监测局部脑氧饱和度的光学技术,前者基于组织光学性质与血红蛋白含量之间关系,后者则基于组织光学性质与脑血流量之间关系[26-27]。除测量脑氧饱和度外,频域近红外光谱和漫反射光谱还可定量测量脑血容量和脑灌注,进而计算脑耗氧量[28],实时测量脑血流量可避免主动脉弓部手术中脑过度灌注。

二、主动脉弓部手术中脑保护策略

主动脉弓部手术中多模态脑监测与管理可辅助改善脑损伤。停循环和选择性脑灌注前后,脑栓塞、脑低灌注或脑过度灌注也可导致一定程度的脑损伤,深低温停循环(DHCA)相关脑损伤程度和机制及脑保护策略仍有待探索。

1.手术策略 脑是对缺氧缺血最敏感的器官,常温下停循环5分钟即发生脑损伤,降温是减少脑代谢的最有效方法。自Griepp等[29]首次报告采用深低温停循环技术成功修复主动脉瘤以来,脑保护的外科技术发生重大变化。《主动脉弓部手术中低温治疗共识》[30]根据术中鼻咽温度分为深低温停循环(14.1 ~ 20.0 ℃)、中低温停循环(MHCA,20.1 ~ 28.0 ℃)和浅低温停循环(MiHCA,28.1 ~ 34.0 ℃)。(1)深低温停循环联合或不联合逆行脑灌注:体温每下降1 ℃,脑代谢率下降6% ~ 7%,深低温停循环20 ~ 30 min是安全时限[31],且这种温度依赖性脑代谢下降在14 ℃以下是最小的,10 ~ 15 ℃脑代谢率仅下降5%[32-33]。与深低温停循环联合逆行脑灌注(16%)和顺行脑灌注(14%)相比,单纯深低温停循环是主动脉弓部手术中最常见的脑保护策略(25%)[34],可提供良好的脑保护,平均停循环时间为(29.7 ± 8.5) min,病死率为2.9%,术后脑卒中和短暂性神经功能障碍发生率分别为2%和5.1%,术后1和5年生存率为92.2%和81.5%[35]。主动脉弓部手术深低温停循环首次联合应用的辅助灌注技术是经上腔静脉逆行脑灌注以清除脑血管内气栓[36]。逆行脑灌注的脑保护机制包括提供代谢底物、清除脑血管内气体和颗粒栓子及维持脑低温,需体外循环机灌注压25 mm Hg以维持脑灌注,压力过高可能造成脑水肿,建议脑灌注流速为150 ~ 300 ml/min以清除代谢产物和栓子碎屑[31]。(2)深低温停循环联合顺行脑灌注:停循环下顺行脑灌注是经右腋动脉、右锁骨下动脉、无名动脉或颈总动脉直接插管或者人工血管吻合等方式,持续顺行灌注经氧合的血液。良好的顺行脑灌注及其监测指标允许更长的停循环时间,以完成复杂的主动脉弓部手术。一项针对5060例主动脉弓部手术患者的Meta分析对比深低温停循环联合顺行与逆行脑灌注的手术疗效,发现两种手术死亡率(5.18%对5.18%)、永久性神经功能障碍(6%对4.7%)和短暂性神经功能障碍(7.5%对8.5%)发生率无明显差异[37]。另一项Meta分析纳入68项临床研究计26 968例行主动脉弓部手术患者,结果显示,与单纯深低温停循环相比,深低温停循环联合顺行或逆行脑灌注与较低的手术死亡率和较少的术后脑卒中发生率相关[38]。上述研究提示单纯深低温停循环可以为短时间停循环的低风险患者提供良好的脑保护,逆行或顺行脑灌注则可以辅助需长时间停循环的复杂主动脉弓部手术中的脑保护。(3)中低温停循环或浅低温停循环联合顺行脑灌注:深低温停循环相关并发症的发生以及脑灌注技术的发展,促使心血管外科医师采用较高停循环温度以改善主动脉弓部手术临床结局。多项研究已证实中低温停循环联合顺行脑灌注的安全性[39-44]。最新一项回顾性研究探究578例行主动脉弓部手术患者中低温停循环联合顺行脑灌注的疗效和安全性,术后30天病死率为6.23%(36/578),脑卒中发生率为5.71%(33/578),短暂性神经功能障碍发生率为5.02%(29/578),术后1年生存率为94%、5年为87%、10年为69%[39]。一项前瞻性研究对比单纯深低温停循环与中低温停循环联合顺行脑灌注的神经系统并发症发生率,发现单纯深低温停循环组术后早期神经系统并发症发生率高于中低温停循环联合顺行脑灌注组[37.93%(11/

29)对13.79%(4/29),$P < 0.05$][40];亦有研究显示这两种脑保护技术对术后认知功能的影响无明显差异[41]。最近调查显示,2/3的欧洲心脏中心倾向双侧顺行脑灌注而非单侧,主要考虑到Willis环不完整可影响脑灌注效果[45]。一项Meta分析对比单侧与双侧顺行脑灌注的疗效和安全性,但并未发现两种技术在术后病死率、短暂性或永久性神经功能障碍方面存在差异[46]。单侧顺行脑灌注可以提供更好的手术显露并减少对脑血管的操作,从而减少栓塞事件的发生;双侧顺行脑灌注则有助于减轻Willis环不完整患者的脑低灌注。深低温停循环曾是主动脉弓部手术的标准术式[47]。目前,脑保护策略已发生重大变化,每种策略各有利弊,主要取决于停循环下最低脑温、停循环时间和脑灌注类型这3种主要因素之间的平衡,并颇具研究前景。(4)避免停循环的脑保护策略:停循环时间较短可以减少术后神经功能障碍已达成一致性意见,但脑温和脑灌注类型仍存争议。有学者报告一种主动脉弓部手术中分支优先技术,即先以直"Y"形人工血管在常温心脏不停跳条件下重建无名动脉、左颈总动脉和左锁骨下动脉,该项技术术中不停止脑组织血供,手术结局良好[48-49],随后陆续在其他心脏中心开展并获得良好疗效,但仅限于少数患者[50-52]。然而该项技术在夹闭左颈动脉和椎动脉过程中可能导致相应脑区缺血,股动脉插管可导致逆行脑栓塞和脑低灌注,主动脉弓上分支的夹闭和操作可能使动脉粥样硬化斑块移位,进而导致脑卒中。因此,分支优先技术的疗效和安全性尚待多中心大样本量临床研究进一步评估。

2. 非手术策略　除上述外科策略外,还有其他非手术策略可以辅助脑保护,包括药物治疗、头部降温及血气管理等方法。(1)药物治疗:多种药物如甘露醇、硫喷妥钠等已用于深低温停循环下脑保护,以降低脑代谢,这些药物须用于停循环前,目的是获得脑电沉默或最低限度脑电活动以实现脑保护[53]。脑灌注受限时,类固醇激素(地塞米松、氢化可的松等)可限制脑水肿以及对复温期间释放的炎性因子的反应。迄今尚无关于深低温停循环下药物治疗的随机对照试验。最近调查显示,几乎所有心脏中心均于深低温停循环下应用至少1种药物,我国常用硫喷妥钠,欧洲国家更常用丙泊酚,糖皮质激素在我国和欧洲国家均常规应用[54]。(2)头部降温:低温停循环下脑低温主要采取低温脑灌注。体外循环下低温脑灌注可能导致不均匀冷却,此时需头部表面降温作为辅助措施,相关研究主要为动物实验[55-57]。有研究对20只仔猪予以75分钟的低温停循环,发现局部头部降温可以降低颅内温度,其7天存活率较未行局部头部降温的仔猪升高(7/10对6/10),但二者脑电变化无明显差异[58];局部头部降温的仔猪脑组织乳酸和丙酮酸/葡萄糖比值明显升高,提示脑代谢紊乱,由此推测,局部头部降温在降低颅内温度的同时可能引起脑代谢紊乱,应谨慎应用。(3)α稳态和pH稳态:α稳态和pH稳态这两种血气管理策略用于监测低温引起的酸碱中毒。pH稳态与继发于脑血管舒张的脑血流量增加、脑氧合能力升高以及脑低温均匀改善有关,尤其适用于儿科心脏手术[59-60]。α稳态在维持脑血流自动调节方面具有优势。一项研究纳入30例于32 ℃下接受冠状动脉旁路移植术的患者,发现α稳态组与pH稳态组脑氧饱和度无明显差异,但pH稳态组复温后出现较严重的酸中毒[61]。2019年,欧洲心胸麻醉协会(EACTA)、欧洲心胸外科协会(EACTS)和欧洲心血管灌注委员会(EBCP)共同发布的《成人心脏手术体外循环指南》[62]建议,在中低温或浅低温下成人心脏手术中采用α稳态进行血气管理。(4)输血:目前尚缺乏高质量循证医学证据支持主动脉弓部手术中预先输注红细胞以提高脑组织携氧能力。一项针对深低温停循环下主动脉弓部手术的回顾性研究探究血红蛋白含量对临床结局的影响,根据红细胞输注阈值分为限制性输血(血红蛋白 < 8 g/dl)和自由输血(血红蛋白 < 10 g/dl),两组术后30天病死率[5.89%(2/34)对7.50%(3/40),$P = 1.000$]和脑卒中发生率[0(0/34)对5%(2/40),$P = 0.500$]均未见明显差异[63],尚待更多研究以探讨输血对脑保护的作用。

综上所述,最低脑温、停循环时间和脑灌注类型对主动脉弓部手术中脑保护至关重要,最短的停循环时间或不停循环是首选,低温是重要组成部分,良好的脑灌注是基础。最佳的脑保护策略需结合围手术期多种因素,制定个体化、多维度的治疗方法。

利益冲突　无

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·小词典·

中英文对照名词词汇(二)

卵圆孔未闭相关性卒中
patent foramen ovale-associated stroke(PFO-AS)
慢性阻塞性肺病
chronic obstructive pulmonary disease(COPD)
矛盾栓塞风险评分
Risk of Paradoxical Embolism Score(RoPE)
美国机械辅助循环支持机构
Interagency Registry for Mechanically Assisted Circulatory Support(INTERMACS)
美国麻醉医师协会
American Society of Anesthesiologists(ASA)
美国神经病学学会 American Academy of Neurology(AAN)
美国食品与药品管理局
Food and Drug Administration(FDA)
美国心血管造影和介入学会
Society for Cardiovascular Angiography and Interventions (SCAI)
美国心脏病学学会 American College of Cardiology(ACC)
美国心脏协会 American Heart Association(AHA)
美国胸外科医师学会 Society of Thoracic Surgeons(STS)
美国胸外科医师学会/美国心脏病学会经导管瓣膜治疗
Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy(STS/ACC-TVT)
美国医学会 American Medical Association(AMA)
目标温度管理 targeted temperature management(TTM)
脑保护装置 cerebral embolic protection device(CEPD)
脑电双频指数 bispectral index(BIS)
纽约心脏协会 New York Heart Association(NYHA)
欧洲经皮心血管介入协会
European Association of Percutaneous Cardiovascular Interventions(EAPCI)
欧洲心胸麻醉协会
European Association of Cardiothoracic Anaesthesiology (EACTA)
欧洲心胸外科协会
European Association for Cardio Thoracic Surgery(EACTS)
欧洲心血管灌注委员会
European Board of Cardiovascular Perfusion(EBCP)
欧洲心血管影像协会
European Association of Cardiovascular Imaging(EACVI)
欧洲卒中组织 European Stroke Organization(ESO)
频域近红外光谱
frequency-domain near-infrared spectroscopy(FD-NIRS)
平均动脉压 mean arterial pressure(MAP)
平均通过时间 mean transmit time(MTT)
浅低温停循环 mild hypothermia circulatory arrest(MiHCA)
桥接移植 bridge-to-transplant(BTT)
深低温停循环 deep hypothermia circulatory arrest(DHCA)
体感诱发电位 somatosensory-evoked potential(SEP)
头痛影响测验-6 Headache Impact Test version 6(HIT-6)
微栓子信号 microembolic signals(MES)
心内超声心动图 intracardiac echocardiography(ICE)
胸腹主动脉瘤 thoracoabdominal aortic aneurysm(TAAA)
血管性血友病因子 von Willebrand factor(vWF)
Toll样受体 Toll-like receptor(TLR)
运动诱发电位 motor-evoked potential(MEP)
中低温停循环
moderate hypothermia circulatory arrest(MHCA)
终末期心力衰竭 end-stage heart failure(ESHF)
阻塞性睡眠呼吸暂停综合征
obstructive sleep apnea syndrome(OSAS)
左心室辅助装置 left ventricular assist device(LVAD)