

# 围手术期脑氧供需和术后认知功能障碍关系的研究进展

尹艳灵 张文凤

201508 上海, 复旦大学附属金山医院手术室

通信作者: 张文凤, Email: wenfengzhangjsyy@126.com

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**【摘要】** 术后认知功能障碍(POCD)是手术后最常见的中枢神经系统并发症之一。新近研究表明, 围手术期脑氧供需变化显著影响 POCD 的发生发展。现探讨围手术期脑氧供在 POCD 中作用的研究进展, 以期预防和治理 POCD 提供新的靶点和方向。

**【关键词】** 术后认知功能障碍; 区域性脑组织氧饱和度; 神经系统并发症; 近红外线光谱仪; 综述

## Research progress on the link between perioperative cerebral oxygen supply and postoperative cognitive dysfunction Yin Yanling, Zhang Wenfeng

Operating Room, Jinshan Hospital Affiliated to Fudan University, Shanghai 201508, China

Corresponding author: Zhang Wenfeng, Email: wenfengzhangjsyy@126.com

**【Abstract】** Postoperative cognitive dysfunction (POCD) is one of the most common post-operative complication of central nervous system. Recent study demonstrates that the changes of cerebral oxygen supply and demand during perioperative period significantly affect the occurrence and development of POCD. This paper discusses the research progress of perioperative cerebral oxygen supply in POCD, which is expected to provide a new target and direction for the prevention and treatment of POCD.

**【Key words】** Postoperative cognitive dysfunction; Regional cerebral oxygen saturation; Complication of central nervous system; Near-infrared spectroscopy; Review

术后认知功能障碍(postoperative cognitive dysfunction, POCD)是指术后逐渐发生的认知功能障碍, 可累及多个认知领域, 包括记忆、执行功能、视空间能力、精神行为等<sup>[1]</sup>。POCD是手术后最常见的中枢神经系统并发症之一, 其发病率为10%~54%, 一般发生在术后数周内, 且老年人高发<sup>[2]</sup>。POCD的高危因素包括糖尿病、术前认知功能障碍病史、肺部疾病、精神障碍疾病史和精神类药物应用、酒精滥用等<sup>[3-5]</sup>。此外, POCD的发病可能和手术类型相关。有研究报道在大型心脏手术术后POCD的发病率可达到30%~80%<sup>[6]</sup>。围手术期很多因素同样被认为和POCD密切相关, 比如麻醉方式和麻醉药物的选择、低血压、神经炎症、脑氧供等<sup>[1]</sup>。有研究发现, 在心脏手术术后, 吸入麻醉患者比全麻患者有更好的认知功能评分<sup>[7]</sup>; 而相比较异丙酚, 术中使用右美托咪啶镇静具有更低的POCD发病率<sup>[8]</sup>。

此外, 术后血清促炎因子(IL-6、IL-8)水平增加和认知障碍明显相关; 相比对照组, POCD患者血清TNF- $\alpha$ 明显升高<sup>[9]</sup>, 提示过度神经炎性反应可能诱发POCD的发生。近年来, 大量的研究提示, 围手术期脑氧供需平衡可能在POCD的发生发展中发挥了重要的作用, 得到了越来越多的关注。

### 一、脑氧和认知功能

大脑占人体总质量的2%, 耗氧量却约占全身耗氧量的20%。脑组织, 尤其是灰质神经元细胞, 在生理状态下主要靠糖代谢供应能量, 对缺氧极度敏感<sup>[10]</sup>。大量的研究已经证实, 在脑缺氧状态下, 认知功能损害和缺氧严重程度呈正相关<sup>[11-12]</sup>。Ochi等<sup>[13]</sup>发现, 在高海拔地区, 外周血氧饱和度和测试者执行功能下降显著相关。脑缺氧导致认知功能下降的原因很复杂, 包括: (1) 线粒体功能对缺氧敏感, 因此脑氧供不足容易导致组织器官能量代谢障

碍<sup>[14]</sup>; (2) 神经递质和酶合成都依赖于充足的氧供。脑缺氧会造成神经递质功能障碍<sup>[15]</sup>, 而很多神经递质, 比如多巴胺和去甲肾上腺素, 都被认为与认知功能相关<sup>[16]</sup>; (3) 在脑缺氧状态下, 脑组织血流会出现重分布; 其大部分血流会供给更原始、更核心的脑区如脑干, 而认知相关的脑组织如海马的供血反而减少, 从而造成认知相关脑组织代谢减低和认知功能损害<sup>[17]</sup>; (4) 缺氧会导致血脑屏障功能障碍<sup>[18]</sup>。正常生理状态下, 血脑屏障与毒性物质的清除, 比如A $\beta$ 的胞外转运以及聚集密切相关, 因此其破坏可能加重既往有认知障碍疾病(如阿尔茨海默病等)脑内的病理损伤, 促进疾病的发展和认知功能恶化<sup>[19]</sup>。

## 二、脑氧和术后认知障碍的发生

### 1. 脑氧代谢的检测方法: 近来越来越多的手段被应用于检测脑组织氧代谢状态, 包括颈静脉球氧饱和度监测、MRI成像技术、PET、近红外线光谱仪(cerebral oximetry uses near-infrared spectroscopy, NIRS)等。颈静脉球氧饱和度(Jugular bulb oxygen saturation, S<sub>jbO<sub>2</sub></sub>)代表脑静脉血氧饱和度, 可通过颈内静脉置管间歇采血或者光纤导管置入颈内动脉球部持续监测, 其正常参考值为54%~75%。其缺点在于有创且反映同侧大脑的整体氧供而非局部脑组织或对侧大脑的氧代谢状况<sup>[20]</sup>。很多基于MR的成像手段, 包括血氧水平依赖(blood oxygenation level dependent, BOLD)成像、自旋标记下的T2弛豫测量(T2-relaxation-under-spin-tagging, TRUST)、磁敏感加权成像(susceptibility weighted imaging, SWI)等, 可以测量脑氧代谢相关参数, 在一定程度上反映脑氧代谢水平。MRI具有安全无创的优点, 但缺点在于耗时相对较长、计算复杂, 限制其临床应用。PET通过外源性放射示踪剂, 包括吸入<sup>15</sup>O<sub>2</sub>气体等来定量检测氧吸收率, 其准确性高, 被认为是金标准, 但其检查费用昂贵<sup>[21]</sup>。NIRS是近年来被用于实时检测区域性脑组织氧饱和度(regional cerebral oxygen saturation, rScO<sub>2</sub>)的常用手段。NIRS的原理是利用氧化血红蛋白和还原血红蛋白对近红外线光波吸收的差异性, 通过计算脑组织的氧化血红蛋白和总血红蛋白的比值, 从而得出监测区域脑组织混合血的氧饱和度, 反映脑氧供状况<sup>[22]</sup>。其缺点在于光穿透性欠佳, 容易受颅骨的影响, 因此目前局限于脑表面皮质区域, 而无法测量深部脑组织氧饱和度<sup>[21]</sup>。NIRS因其操作便利的优点, 被广泛应用于围手术期脑氧饱和度的监测。

### 2. 脑缺氧和POCD: 围手术期脑组织缺氧与POCD发病有密切的关系。有研究报道, 术中rScO<sub>2</sub>最低值<50%<sup>[23]</sup>和<35%<sup>[24]</sup>与POCD发病有显著的关系。POCD在心脏术后发生率较高, 可能和术中脑组织容易缺血缺氧相关。Momeni等<sup>[25]</sup>对1 513例心脏介入术患者进行了分析, 将术后MMSE评分下降>2分或3个月及6个月时出现认知能力下降定义为POCD。他们发现术中脑电图抑制程度和术后rScO<sub>2</sub>水平与术后谵妄以及POCD的发生显著相关。一项Meta分析显示, 术中脑氧监测有助于减少术后1周内POCD的发生; 相比对照组, 监测组MMSE评分更高, 同时监测组ICU住院时间更短<sup>[26]</sup>。Soenarto等<sup>[27]</sup>的研究则发现, 在心脏手术中, POCD的发生和rScO<sub>2</sub>的绝对值没有显著关系, 而和术中rScO<sub>2</sub>的降幅(大于基线值的20%)密切相关, 提示术中监测rScO<sub>2</sub>可能对避免心脏手术POCD的发生有潜在的益处。

在非心脏手术中, Nielsen<sup>[28]</sup>的研究发现, 单肺通气的胸外科手术、大腹部手术、髋关节手术和部分腹腔镜手术会出现rScO<sub>2</sub>降低; 此外, 在胸外科、骨科大手术和腹部手术中, POCD的发生可能与术中rScO<sub>2</sub>下降有关。rScO<sub>2</sub>下降>20%~25%可能预测POCD的发生, 因此作者认为干预的阈值界定在rScO<sub>2</sub>下降>10%。崔凡等<sup>[29]</sup>对128例肺叶切除的患者, 采用组织氧饱和度仪监测双侧前脑组织氧饱和度(Sc<sub>t</sub>O<sub>2</sub>), 发现单肺通气期间Sc<sub>t</sub>O<sub>2</sub>最低值是发生POCD的危险因素。Tomaszewski等<sup>[30]</sup>的研究则发现, 在全髋关节置换手术中, 术中rScO<sub>2</sub>水平下降可能和脑微栓塞事件以及术后POCD的发生密切相关, 提示rScO<sub>2</sub>可以作为预测POCD发生的一项重要指标。朱凯等<sup>[31]</sup>在进行主动脉弓部手术的成人患者中发现, 术中采用NIRS监测rScO<sub>2</sub>, 左侧rScO<sub>2</sub>降低是术后神经系统并发症、POCD发生的危险因素, 尤其是当rScO<sub>2</sub><55%时更易发生。综上所述, 围手术期脑组织缺氧是POCD发病重要的预测因子。在术中密切监测脑组织的氧代谢状态, 对避免POCD的发生具有重要的意义。

### 3. 脑高氧和POCD: 术中过高的吸入氧浓度(FiO<sub>2</sub>) (0.8~1.0)吸入具有“双刃剑”效应。以往的研究认为术中吸入高浓度氧可以降低术后伤口感染的概率, 具有抗感染的作用, 尤其是在直肠手术中<sup>[32]</sup>。然而, 过高的FiO<sub>2</sub>同时可能增加术后的长期(>2年)死亡率和不良预后的发生<sup>[33-34]</sup>。围手术期脑组织过高的氧浓度可以导致氧自由基形成和氧化应激反

应、加重炎性损伤、降低肺换气、减少微血管灌注,从而损伤神经元细胞,导致脑组织损伤<sup>[35]</sup>。新近研究表明,相比较术中吸入过高的FiO<sub>2</sub>,监测和维持正常水平的氧供,可以减少POCD的发生<sup>[36]</sup>。目前关于高氧和POCD的报道非常少,需要更多的研究来进一步证实。

### 三、改善脑组织氧饱和度可能预防POCD的发生

1. 麻醉方式的选择和POCD:近年来研究证实,麻醉方式的选择对术中脑组织氧饱和度水平有重要的影响。有研究报道,在心脏搭桥手术前,七氟醚吸入麻醉对术中SjvO<sub>2</sub>的稳定和脑氧供需平衡有明显益处,术后患者外周血脑损伤指标S100B和神经元特异性烯醇化酶(NSE)浓度明显降低,术后24h简易智能精神状态量表(MMSE)评分要显著高于非七氟醚吸入麻醉组<sup>[37]</sup>。Du等<sup>[38]</sup>则发现,在腹腔镜胆囊切除术中,术前使用帕瑞昔布联合手术中使用右美托咪啶可以提高术中SjvO<sub>2</sub>和静脉血氧饱和度(PjvO<sub>2</sub>)水平,减轻术后疼痛程度,改善MMSE评分。在儿童全麻手术中,相较于地佐辛,右美托咪啶可以有效地避免血氧饱和度(SaO<sub>2</sub>)下降,维持术中SaO<sub>2</sub>水平,同时减少POCD的发生<sup>[39]</sup>。另有研究显示,对于老年患者的冠状动脉搭桥手术,右美托咪啶能减少单肺通气中脑组织氧饱和度ScT(O<sub>2</sub>)水平的波动和下降;相比较生理盐水对照组,其72h和7d的MMSE评分显著升高<sup>[40]</sup>。因此,麻醉方式的选择可能通过调控脑组织氧合水平,影响POCD的发生发展,应加以重视。

2. 术中脑组织氧饱和度的监测管理和POCD:当术中脑组织氧饱和度降低时,可以通过不同的手段来维持脑组织氧合水平。常用干预措施包括改变头位;扩容或使用血管升压药物提高血压;改变呼吸机参数来优化SaO<sub>2</sub>和PaCO<sub>2</sub>水平,避免过度通气;改善心脏功能,增加泵流量,保持心脏指数>2 L/(m<sup>2</sup>·min);在贫血时给予输血治疗;通过多种措施(改变麻醉深度等)来减少脑耗氧量。这些措施可以有效地提高rScO<sub>2</sub>,改善术中脑缺氧<sup>[41]</sup>。

越来越多的研究证实,当围手术期发生脑缺氧时,通过不同手段来改善脑组织氧供,可以有效减少POCD的发生。Rogers等<sup>[42]</sup>发现,在心脏手术中,相比较未监测组,监测组通过保持术中rScO<sub>2</sub>>50%或70%的基础水平,可以改善患者3个月后认知评分,尤其在语言流畅性方面有显著提高。另有报道采用不同的方式(改变头位、增加术中FiO<sub>2</sub>、增加麻醉深度、降温等),保持rScO<sub>2</sub>大于患者基础水

平的80%或绝对值的50%,能显著降低冠状动脉搭桥POCD的发生率<sup>[43]</sup>。一项Meta分析提示,在冠状动脉搭桥术中,监测和维持脑氧饱和度可以有效地避免POCD事件的发生<sup>[44]</sup>。此外,Mohandas等<sup>[45]</sup>的研究发现,当监测术中rSO<sub>2</sub><50%或基线值的80%,通过改变头位、提高FiO<sub>2</sub>、减少脑耗氧量(改变麻醉深度、降温等)等措施提高rSO<sub>2</sub>,能有效地减少体外循环手术POCD的发生。

在非心脏手术中,改善脑组织缺氧同样可以降低POCD的发生率。有研究发现,在颈动脉内膜剥脱术中,相比较静脉全麻,七氟醚维持麻醉可以抑制单侧脑氧饱和度下降以及双侧大脑半球的氧供不对称,进一步改善患者术后第5天的蒙特利尔认知评估量表(MOCA)评分和认知能力<sup>[46]</sup>。Murniece等<sup>[47]</sup>对24例脊髓手术患者进行前瞻性研究,通过NIRS设备(INVOS 4100)进行脑组织氧饱和度监测。当双侧或单侧rScO<sub>2</sub>下降幅度>20%的基线水平或降幅绝对值>50%时,如果通过不同的手段来改善脑氧合状况,包括摆放头位或者注射麻黄碱提高平均动脉压等,可以有效地提升rScO<sub>2</sub>水平,降低POCD的发生率,从而改善患者的认知能力。另有研究发现,在80例老年患者的脊髓手术中,通过羟乙基淀粉进行扩容和血液稀释,可以明显提高血容量,降低动静脉血氧含量差、脑氧摄取量和代谢率,同时术后1d MMSE评分要显著高于对照组,而脑损伤标记物S100B和NSE水平要低于对照组,提示其具有潜在的改善术后认知功能的作用<sup>[48]</sup>。此外,Ballard等<sup>[49]</sup>发现,在60岁以上行骨科或腹部手术的老年患者中进行脑氧饱和度监测和管理,1周、12周以及52周后患者POCD发生率明显下降,MMSE评分以及执行功能明显提高。综上所述,维持和改善术中脑组织氧饱和度水平,避免脑组织氧饱和度过低、降幅过大或过高的氧供,有望成为POCD有效的预防手段。

综上所述,围手术期脑组织氧供需和POCD的发生密切相关。脑组织氧饱和度过低、降幅过大、过高等状况均可能诱发POCD的发生,加重术后认知功能障碍。然而,如何监测和维持围手术期脑组织氧合水平仍有待进一步研究;此外,NIRS在POCD中的应用缺乏高质量的研究证据<sup>[51]</sup>,而更精确的脑氧代谢的检查手段,包括MRI、PET,因其各种局限性,也很少被应用于术中。因此,更多高级别的、在不同人群中(心脏手术、非心脏手术、老年

患者、儿童等)的相关随机对照试验研究需要在将来进一步开展。监测和维持围手术期脑组织氧供,有望成为预防和治疗 POCD 发病的新手段,具有潜在的、重要的临床应用价值。

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