

间隔收缩-舒张向左移位,从而阻碍左心室的充盈和排出^[7],导致左心室射血分数降低,继而出现全身性低血压^[8]。全身性低血压又可导致右心室冠状动脉灌注降低、心肌缺血。这种恶性循环称为“右心室死亡螺旋”^[5],是导致高危肺栓塞循环衰竭的原因。

动脉-静脉体外膜氧合(veno-arterial extracorporeal membrane oxygenation, VA-ECMO)似乎是打破“右心室死亡螺旋”的最佳选择^[5]。首先,VA-ECMO可迅速恢复血流动力学稳定性并提供充分的气体交换;其次,VA-ECMO可显著改善右心室功能不全,通过插管可减轻右心室负荷,使右心室舒张末期容积、压力和心肌耗氧量减少,右心室供氧和需氧达到平衡;VA-ECMO恢复循环稳定后,机体平均动脉压升高可提高冠状动脉灌注压,显著改善右心室功能,最终恢复器官有效灌注^[5]。静脉-静脉体外膜氧合(veno-venous extracorporeal membrane oxygenation, VV-ECMO)也可改善氧合和清除CO₂,降低肺动脉血管阻力,从而改善右心室功能。在特定的情况下,VV-ECMO也可以改善呼吸性酸中毒和过度通气导致右心衰竭的高危肺栓塞^[9]。

2 高危肺栓塞再灌注治疗及 ECMO 应用现状

高危肺栓塞病死率高,多在出现症状1 h内死亡,早期恢复血流动力学稳定、降低肺动脉压可以提高患者生存率^[2]。肺栓塞的常规治疗方法包括适当补液、血管活性药物应用、呼吸机辅助通气、抗凝、静脉溶栓、导管定向溶栓和外科手术取栓治疗等^[2]。常规治疗失败和需要进一步治疗的患者常需要机械辅助维持循环稳定^[10-11],ECMO是首选的机械辅助手段,其可维持患者全身氧供和血流动力学相对稳定,保证重要器官的灌注,为进一步的再灌注治疗赢得时间^[12]。

1961年,COOLEY等^[13]首次应用ECMO成功治疗了高危肺栓塞,之后ECMO在高危肺栓塞中的临床应用明显增加。2019年欧洲心脏病学会发布的指南提出:发生难治性循环衰竭或心脏骤停的肺栓塞患者,可考虑给予ECMO联合手术取栓或导管定向溶栓治疗^[14]。但目前国内外应用ECMO治疗肺栓塞仍处于探索阶段,已发表的研究多为个案报道、回顾性研究及荟萃分析,且各研究报道的患者存活率差别较大。从现有的文献报道来看,ECMO可使发生心脏骤停(cardiac arrest, CA)的肺栓塞患者获得明确的生存获益,随着血流动力学的稳定和氧

合的改善,ECMO可为高危肺栓塞患者进一步治疗提供更多的时间和机会^[15-16]。

3 ECMO 为高危肺栓塞再灌注治疗提供时机

ECMO单独用于治疗高危肺栓塞的研究很少,而且多数研究认为ECMO不能单独治疗肺栓塞^[12,17-18];但是ECMO联合抗凝治疗可使70%的患者得以康复^[19-20]。肝素抗凝诱导的血栓溶解和自发性纤维蛋白溶解可以改善肺动脉梗阻,通过抗凝有可能实现ECMO早期撤机^[18]。若存在严重右心室功能障碍,仅通过ECMO联合抗凝治疗心脏功能恢复较慢,一般需联合其他治疗手段(如静脉溶栓式导管定向溶栓)^[14]。有研究发现,无溶栓禁忌的患者采用ECMO联合静脉溶栓或导管定向溶栓可快速逆转右心室扩张和右心功能障碍、恢复血流动力学稳定,提高患者存活率^[21]。不能接受静脉溶栓治疗的患者可选择导管定向溶栓治疗^[22],溶栓治疗失败的患者仍可选择外科栓塞切除治疗^[23]。

不宜常规溶栓或需要手术迅速解除梗阻的高危肺栓塞患者,ECMO可以迅速降低右心室负荷、稳定血流动力学并改善氧合^[4,24]。研究表明,早期行肺栓塞切除术对于降低术后复发性肺栓塞和肺动脉高压有积极作用^[9,25]。然而,对循环不稳定的肺栓塞患者进行复杂的手术可能会增加发生并发症的风险,在等待肺动脉血运重建的同时保持足够的冠状动脉流量和脑氧合对提高患者的生存率和生活质量至关重要^[25-26]。ECMO作为高危肺栓塞治疗和术后恢复的桥梁,已成为急慢性血栓栓塞性疾病患者管理的一个重要组成部分^[16]。ECMO的使用率从2005年的0.07%上升到2013年的1.10%,随着使用率的升高,高危肺栓塞患者的院内病死率明显降低^[13,27]。过去20 a,高危肺栓塞患者给予ECMO治疗后总生存率可高达70.1%^[28],其生存率高低与不同联合治疗的选择(联合抗凝治疗、静脉溶栓,或者外科手术治疗)无明显相关性^[29]。

4 ECMO 的应用时机、适用人群及模式选择

目前,关于ECMO上机时机的界定仍然比较模糊,黎嘉嘉等^[30]建议对高风险肺栓塞患者尽早启动循环和呼吸支持,建议在确诊30 min内进行插管,并在迅速稳定患者病情后进行溶栓或血栓切除术等治疗。研究发现,早期应用ECMO提供稳定的循环支持可以降低患者病死率^[31],越早使用ECMO,患

者生存获益越大^[32]。因此,不同文献报道的高危肺栓塞患者生存率参差不齐,可能与 ECMO 使用时机不同有关^[33]。

由于 ECMO 使用费用昂贵,并且需要专门的设备和训练有素的体外循环管理团队,因此 ECMO 的适应证、适用人群的选择一直是个难题。2019 年美国心脏协会报道称尚未发现足够的证据证明心脏骤停患者可常规使用体外心肺复苏 (extracorporeal cardiopulmonary resuscitation, ECPR),但当常规心肺复苏 (cardiopulmonary resuscitation, CPR) 失败时,可考虑使用 ECPR 提供循环支持^[34]。高危肺栓塞引起的心脏骤停是可逆的,尽早进行 ECPR 可显著提高心脏骤停患者的自主循环恢复率和神经功能预后^[6,35]。一项大型多中心欧洲队列研究在评估了不同人群使用 ECPR 后的生存率和神经功能恢复情况后提出,制定更严格的 ECPR 选择标准 (年龄 ≤ 65 岁;有旁观者目睹心脏骤停并进行 CPR;无终末期疾病;在心脏骤停后 1 h 内启动 ECMO) 可使患者获得更好的治疗效果^[36]。有研究提出,对高危肺栓塞患者进行风险评分,筛选出适合进行 ECMO 的患者,对提高 ECMO 成功率至关重要^[30]。

无论是 VV-ECMO 还是 VA-ECMO 都可以迅速改善低氧血症和高碳酸血症,减轻心脏前负荷、降低室壁张力,为右心室提供间接支持。但目前大多数研究是关于 VA-ECMO 联合治疗方案,关于 VV-ECMO 模式的研究相对较少^[37-38]。KMIEC 等^[9]将 75 例高危肺栓塞患者分为 VA-ECMO 组 ($n = 46$) 和 VV-ECMO 组 ($n = 29$),结果发现,2 组患者的出院存活率比较差异无统计学意义;该研究还发现,ECMO 支持下循环稳定后接受血栓切除手术和仅接受抗凝治疗的患者出院时的存活率比较差异无统计学意义。STADLBAUER 等^[6]将 119 例需要 ECMO 循环辅助的心源性休克患者分别给予 VA-ECMO (87 例) 或 VV-ECMO (32 例),结果发现,患者的总生存率为 45.4% (54/119),2 组患者的生存率比较差异无统计学意义。

5 结论

ECMO 可通过迅速恢复血流动力学稳定性、改善右心室功能,为高危肺栓塞再灌注治疗提供时机。通过成立多学科肺栓塞救治团队汇聚不同学科专家团队前瞻性评估病情严重程度和危险分级,选择更合适的植入时机和 ECMO 模式,可有效提高救治效率、改善临床结局^[4,16,39]。前瞻性、多中心大规模研究来评估 ECMO 在高危肺栓塞患者中的作用可能会成为新的研究热点。

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