·泛血管医学时代“脑心同治”手术·

终末期心力衰竭左心室辅助装置植入术后神经系统并发症的危险因素

李志朋 王伟

【摘要】 左心室辅助装置植入术是除心脏移植外治疗终末期心力衰竭的有效手段，术后易发生神经系统并发症，以缺血性和出血性卒中常见。本文综述常见的左心室辅助装置植入术后神经系统并发症并总结其危险因素，提出早期预防及管理策略，为终末期心力衰竭左心室辅助装置植入术围手术期和长期管理提供指导。

【关键词】 心力衰竭； 心室； 心脏辅助装置； 手术后并发症； 神经系统疾病； 综述

Neurological complications risk factors in end-stage heart failure patients after left ventricular assist devices implantation

LI Zhi-peng, WANG Wei

Department of Intensive Care Unit, TEDA International Cardiovascular Hospital, Tianjin 300457, China

Corresponding author: WANG Wei (Email: wangwei_wzxyy@sina.com)

【**Abstract**】 Left ventricular assist devices (LVAD) implantation is an effective treatment for end-stage heart failure in addition to heart transplantation. Neurological complications, especially ischemic stroke and hemorrhagic stroke, are the most common complications in patients after LVAD. This paper reviews the common neurological complications and its risk factors in patients after LVAD, and proposes early prevention and management strategies to provide guidance for the perioperative and long-term management of LVAD implantation in end-stage heart failure.

【**Key words**】 Heart failure; Heart ventricles; Heart-assist devices; Postoperative complications; Nervous system diseases; Review

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终末期心力衰竭(ESHF)患者病情复杂且病死率高，临床缺少药物治疗方法，心脏移植是有效治疗手段，但是由于供体短缺，使大部分患者失去救治机会。应用左心室辅助装置(LVAD)进行机械循环支持是现阶段终末期心力衰竭的有效治疗方法，1年生存率是应用正性肌力药、肾素-血管紧张素系统(RAS)抑制药、β受体阻断药、醛固酮受体阻断药等传统药物的2倍以上[1]；且随着技术的进步，左心室辅助装置已由最初作为等待心脏移植的过渡治疗(即桥接心脏移植)发展成为终末期心力衰竭的永久性替代治疗。近年来，治疗终末期心力衰竭的机械循环支持装置在国内迅速发展，尤其是左心室辅助装置的应用日益广泛，使得左心室辅助装置植入术后并发症受到越来越多的关注。应用传统药物治疗的终末期心力衰竭患者因脑低灌注出现缺血性卒中、记忆力减退、痴呆等神经系统并发症[2-3]；行左心室辅助装置植入术的患者则因连续血流动力学改变和术后抗凝策略出现消化道出血、右心衰竭、高血压、血栓或出血、感染、电解质紊乱等并发症[4-7]，尤以血栓和出血最易引发神经系统并发症如缺血性或出血性卒中、短暂性脑缺血发作(TIA)、运动障碍或认知功能障碍等[8-11]，且神经系统并发症

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作者单位：300457 天津，泰达国际心血管病医院重症监护病房

通讯作者：王伟，Email：wangwei_wzxyy@sina.com

是患者的首位死因[12]，与未发生缺血性或出血性卒中的患者相比，并发缺血性和出血性卒中的患者病死风险分别增加4.8和18倍[13]，因此，有效预防左心室辅助装置植入术后神经系统并发症对提高终末期心力衰竭患者生存率至关重要。随着左心室辅助装置植入后应用时间的延长，术后神经系统并发症发生率逐渐增加；加之左心室辅助装置植入后连续性血流与正常心脏血流动力学不同，故此类患者的管理目标和策略与常规心脏手术和心脏移植手术不尽一致。本文拟综述常见的左心室辅助装置植入术后相关神经系统并发症并总结其危险因素，探究早期预防方法，以为终末期心力衰竭患者左心室辅助装置植入术围手术期和术后长期管理提供理论依据和临床指导。

一、左心室辅助装置植入术后神经系统并发症

目前应用的第2代连续血流泵主要包括以HMⅡ（HeartMate Ⅱ）为代表的轴流泵和以HVAD（HeartWare Ventricular Assist Device）为代表的离心泵，以HM3（HeartMate 3）为代表的第3代磁悬浮离心泵也已应用于临床。随着泵的设计理念和技术不断改进，神经系统并发症逐渐减少，仍有部分患者术后出现严重神经系统并发症特别是缺血性和出血性卒中，极大威胁患者生命。2020年，美国机械循环支持机构（INTERMACS）的报告指出，应用第2代连续血流泵的左心室辅助装置植入术后90天内脑卒中发生率为6.3%，90天后脑卒中发生率为4.1%[14]。HMⅡ属于轴流式左心室辅助装置，运行时轴承间隙难免进入血液，使轴承与血液直接接触，破坏全血细胞，导致轴承及其附近易形成血栓。一项以桥接心脏移植为目的多中心临床研究显示，HMⅡ植入后脑卒中发生率为8.90%（25/281），且缺血性卒中发生率高于出血性卒中[5.34%（15/281）对3.20%（9/281）][15]。另一项HMⅡ多中心临床研究纳入134例以永久性替代治疗为目的的终末期心力衰竭患者，为期2年的随访中脑卒中发生率为17%，其中出血性卒中是死亡的最主要原因（9%）[16]。与HMⅡ同期出现的HVAD为离心式左心室辅助装置，通过流体动力悬浮技术避免血液与轴承直接接触，设计者最初认为此种设计方式可以减少血栓和出血事件的风险，但高速血流可产生高剪应力，破坏全血细胞和血管内皮细胞，甚至引起更多的脑卒中事件。ENDURANCE试验（试验编号：NCT01166347）显示，HVAD植入后脑卒中发生率高于HMⅡ[29.73%（88/296）对12.08%（18/149），$P<0.001$]，其中缺血性卒中[17.57%（52/296）对8.05%（12/149），$P=0.007$]和出血性卒中[14.86%（44/296）对4.03%（6/149），$P<0.001$]均高于HMⅡ，且大多数脑卒中发生于HVAD植入后6个月内[17]。随后的ENDURANCE补充试验发现，实施血压管理方案的患者HVAD植入后出血性卒中发生率减少50%[18]。2014年，HM3的问世引入了磁悬浮技术，该技术无需血流压力支撑，血液在泵腔内的悬浮间隙更大，显著减少脑卒中发生率。MOMENTUM3试验（试验编号：NCT02224755）显示，植入HM3的患者总体脑卒中[10.05%（19/189）对19.19%（33/172），$P=0.020$]和缺血性卒中[6.35%（12/189）对13.37%（23/172），$P=0.030$]发生率均低于植入HMⅡ的患者，而二者出血性卒中发生率无明显差异[4.23%（8/189）对9.30%（16/172），$P>0.05$][19]；特别是HM3植入后脑卒中发生率较HMⅡ降低约50%，致残性卒中发生率也较HMⅡ显著减少[20]。INTERMACS研究纳入6205例左心室辅助装置植入术后患者，发现植入HM3的患者术后12个月缺血性卒中（3.4%对7.7%，$P<0.001$）和出血性卒中（2.0%对7.2%，$P<0.001$）发生率均低于植入HVAD的患者[21]。因此，2021年美国食品与药品管理局（FDA）紧急停止HVAD的临床应用[22]。一项纳入683例左心室辅助装置植入术后患者的研究显示，73例术后并发出血性卒中，以脑实质出血为最常见亚型（71.23%，52/73），其次为蛛网膜下腔出血（31.51%，23/73）和硬膜下出血（23.29%，17/73），约21.92%（16/73）的出血性卒中患者为多种亚型并存[11]。2021年，由泰达国际心血管病医院和航天泰心科技有限公司联合自主研发的HeartCon第3代磁液悬浮离心式左心室辅助装置顺利完成多中心临床试验，截至2022年有超过50例患者植入HeartCon，其中泰达国际心血管病医院治疗的20例患者中仅1例术后并发出血性卒中[23-24]。此外，终末期心力衰竭患者左心室辅助装置植入术后还可出现短暂性脑缺血发作、认知功能障碍等神经系统并发症[25-26]。研究显示，植入HMⅡ后30天，2.14%（6/281）患者并发短暂性脑缺血发作，5.34%（15/281）并发癫痫、谵妄等神经精神疾病，5.69%（16/281）出现心理障碍[15]；植入HVAD后，8.45%（25/296）的患者并发短暂性脑缺血发作[17]；植入HM3后，约3.17%（6/189）患者并发短暂性脑缺血发作，3.17%（6/189）并发神经功能障碍，2.65%（5/189）

并发惊厥发作[19]。亦有研究发现,约23%的终末期心力衰竭患者左心室辅助装置植入术后并发认知功能减退[26],进一步增加脑卒中和死亡风险[27]。应注意的是,对出现神经系统并发症的患者进行严格评估有利于预测终末期心力衰竭患者预后。美国国立卫生研究院卒中量表(NIHSS)广泛用于脑卒中严重程度的评估,左心室辅助装置植入术后脑卒中患者NIHSS评分<7分提示预后较好[28]。改良Rankin量表(mRS)亦用于神经功能损伤程度的评估,INTERMACS研究对1515例左心室辅助装置植入术后脑卒中患者进行分析发现,术后并发脑卒中1个月时mRS评分4~5分的患者6个月内病死率接近40%[29]。

二、左心室辅助装置植入术后神经系统并发症的危险因素

1.社会人口学因素 神经系统疾病很大程度受患者自身因素影响,包括性别、年龄、生活方式、基础疾病等社会人口学因素。(1)性别:性别对左心室辅助装置植入术后神经系统并发症的影响较为明确。女性术后更易并发神经系统疾病:植入HMⅡ的患者中女性发生出血性卒中(HR=1.450,95%CI:1.140~1.840;P=0.022)和缺血性卒中(HR=1.880,95%CI:1.100~3.340;P=0.021)的风险均较男性增加[30];INTERMACS研究显示,女性术后并发脑卒中的总体风险比为1.530(95%CI:1.320~1.770,P<0.001)[31]。(2)年龄:行左心室辅助装置植入术的患者年龄与术后神经系统并发症具有相关性,年龄越大、术后发生神经系统并发症的风险越高(HR=1.300,95%CI:1.040~1.630;P=0.020)[32]。此外,随着年龄的增长,糖尿病和高脂血症等代谢性疾病的发生率增加,均增加左心室辅助装置植入术后脑卒中风险。(3)生活方式:不良生活方式如吸烟可增加左心室辅助装置植入术后脑卒中风险,左心室辅助装置植入术后2年内吸烟患者脑卒中发生率为39%,远高于不吸烟和戒烟患者[33]。(4)基础疾病:研究显示,合并房颤的终末期心力衰竭患者左心室辅助装置植入术后血栓事件(缺血性卒中、短暂性脑缺血发作、溶血或泵血栓形成)风险显著增加(HR=1.890,95%CI:1.300~2.900;P=0.002)[34];既往有糖尿病病史的患者术后发生缺血性卒中的风险比为1.990(95%CI:1.190~3.340,P=0.009)[30]。

2.术后血压 无论是轴流泵还是离心泵均改变左心室辅助装置植入术后血流动力学模式,因此,合理控制术后平均动脉压(MAP)和收缩压(SBP)对减少神经系统并发症至关重要。研究显示,接受长期机械循环支持的患者中高血压组脑卒中发生率高于非高血压组(16%对7%),其中高收缩压患者脑卒中风险是非高收缩压患者的2.51倍(95%CI:1.150~5.450,P=0.022)[35];左心室辅助装置植入术后平均动脉压>90 mm Hg的患者脑卒中发生风险高于<80 mm Hg患者(HR=2.800,95%CI:1.090~7.170;P<0.05)[36]。INTERMACS研究显示,左心室辅助装置植入术后控制平均动脉压≤75 mm Hg且收缩压<90 mm Hg可降低死亡风险[37]。

3.凝血功能 缺血性卒中的重要危险因素之一是泵血栓形成,可能与非生理性血流、抗凝治疗不充分和全身高凝状态致血栓形成有关。左心室辅助装置植入术后需常规抗凝治疗,推荐国际标准化比值(INR)维持于2~3[38];若抗凝治疗不充分,极易形成血栓特别是泵血栓,导致缺血性卒中。一项针对左心室辅助装置植入术后缺血性卒中的单中心回顾性研究显示,术后约1/3的缺血性卒中继发于泵血栓形成[39]。尽管随着设备和技术的改进,泵血栓形成率显著降低,但仍有2%~13%患者术后发生泵血栓形成[14],推测与术后抗凝治疗不充分有关,左心室辅助装置植入术后发生缺血性卒中的患者中约47.4%为亚抗凝治疗(INR<2)[13,40],进一步增加缺血性卒中的风险(OR=4.800,95%CI:1.600~14.400;P=0.010)[13]。然而,左心室辅助装置植入术后应用抗凝药亦可增加出血性卒中的风险,与仅接受抗凝治疗但未行左心室辅助装置植入术的患者相比,行左心室辅助装置植入术的患者发生出血性卒中的风险更高[41]。多项研究表明,轴流泵可诱发左心室辅助装置植入术后出现不同程度的获得性血管性血友病因子病[42-44],而血管性血友病因子缺陷可导致血小板激活、黏附和聚集能力下降,引起轻微出血或大出血[45],导致出血性卒中。

4.感染 感染亦是左心室辅助装置植入术后常见并发症,发生率约为39%,是导致术后死亡的重要原因[14]。一项单中心回顾性研究显示,左心室辅助装置植入术后感染相关脑卒中发生率为12.66%(20/158),且通常发生于感染后4天,其中最常见的感染类型是菌血症(27%)、泵导线感染(17%),其次是手术切口感染(8%)和泵腔感染(6%)[46]。INTERMACS研究也表明,感染可显著增加脑卒中风险,特别是左心室辅助装置植入术后感染可使脑

卒中风险升高8倍[31,47]。左心室辅助装置植入术后感染导致脑卒中的机制可能与感染性心内膜炎、脓毒症相关性脑病(SAE)、真菌性动脉瘤和脑血管炎相关[39,46-48]。此外,左心室辅助装置植入术后的非搏动性连续血流可引起血管内皮细胞损伤,更易发生真菌黏附和真菌血症[49]。

5.动脉粥样硬化 动脉系统受收缩和舒张相关周期性剪应力的作用,有助于维持外周血管正常功能[50]。左心室辅助装置植入术后的非搏动性连续血流对血管内皮细胞产生高剪应力,导致其功能损害,使动脉僵硬度增加,形成类似重度主动脉粥样硬化的血流动力学模式,增加脑卒中风险[10,51-52]。与健康人群和搏动性血流左心室辅助装置植入术后患者相比,左心室辅助装置植入术后发生非搏动性连续血流的患者主动脉僵硬度更高,主动脉粥样硬化后缺血性和出血性卒中的发生率均增加[53]。

三、左心室辅助装置植入术后神经系统并发症的预防

左心室辅助装置植入术后神经系统并发症通常发病急骤、进展迅速,病死率和病残率均较高,应早期预防[54]。性别、年龄、生活方式(吸烟)、基础疾病(房颤、糖尿病、高血压等)均与左心室辅助装置植入术后神经系统并发症密切相关,故术前应进行详细的病史采集、体格检查、实验室检查和心肺功能评估,有效控制血压、血糖、血脂并戒烟,以降低术后神经系统并发症风险[55-56]。此外,术中尽量减少主动脉阻断和体外循环时间,减少二尖瓣成形术、主动脉瓣成形术等伴随心脏手术的数量,以减少对血管内皮细胞和动脉系统的损伤,降低术后脑卒中风险[56-57]。最重要的预防措施应属围手术期和术后长期管理[7]。首先应预防血栓和出血,合理有效的抗凝治疗不可或缺[27]。2013年,国际心肺移植协会(ISHLT)建议,行左心室辅助装置植入术的患者应长期应用阿司匹林(81~325 mg)和华法林,维持INR于2~3[58-60];治疗过程中应定期监测INR,结合个体危险因素,在血栓与出血之间达到平衡[30,61]。此外,还应积极控制血压和预防感染,左心室辅助装置植入术后特殊血流动力学模式要求患者须长期保持平稳的低平均动脉压和收缩压[62-63],故围手术期应调整适宜泵速,且术后应用降压药以控制血压;持续性血流可造成血管内皮细胞损伤,增加感染风险,故长期支持治疗中应定期检查,尤其是导线周围皮肤状况,以预防和及时控制感染[64-65]。

终末期心力衰竭患者左心室辅助装置植入术后易发生神经系统并发症,尤其是缺血性和出血性卒中,常导致患者预后不良。临床可通过术前对患者各系统情况全面评估,术后对血压、凝血功能、感染和动脉粥样硬化的控制以及对患者的严格评估,有效预防或减少神经系统并发症,改善预后。

利益冲突 无

参 考 文 献

[1] Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, Long JW, Ascheim DD, Tierney AR, Levitan RG, Watson JT, Meier P, Ronan NS, Shapiro PA, Lazar RM, Miller LW, Gupta L, Frazier OH, Desvigne-Nickens P, Oz MC, Poirier VL; Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group. Long-term use of a left ventricular assist device for end-stage heart failure[J]. N Engl J Med, 2001, 345:1435-1443.

[2] Agrawal S, Nijs K, Subramaniam S, Englesakis M, Venkatraghavan L, Chowdhury T. Predictor role of heart rate variability in subarachnoid hemorrhage: a systematic review[J]. J Clin Monit Comput, 2023.[Epub ahead of print]

[3] Massaro AR. Neurological complications of heart failure[J]. Handb Clin Neurol, 2021, 177:77-89.

[4] Hammer Y, Bitar A, Aaronson KD. Gastrointestinal bleeding on continuous-flow left ventricular assist device therapy[J]. ESC Heart Fail, 2023, 10:2214-2224.

[5] Krishnarao K, Krim SR. Management of hypertension in patients supported with continuous flow left ventricular assist devices[J]. Curr Opin Cardiol, 2023, 38:281-286.

[6] Siems C, Aggarwal R, Shaffer A, John R. Right heart failure after left ventricular assist device implantation: a persistent problem[J]. Indian J Thorac Cardiovasc Surg, 2023, 39(Suppl 1):161-169.

[7] Morshuis M, Fox H, Lauenroth V, Schramm R. Long-term assist device patients admitted to ICU: tips and pitfalls[J]. J Intensive Med, 2022, 3:81-88.

[8] Hernandez NS, Kanter M, Sharma V, Wang A, Kiernan M, Kryzanski D, Heller R, Nail T, Riesenburger RI, Kryzanski JT. Radiographic risk factors for intracranial hemorrhage in patients with left ventricular assist devices[J]. J Stroke Cerebrovasc Dis, 2022, 31:106869.

[9] Malone G, Abdelsayed G, Bligh F, Al Qattan F, Syed S, Varatharajullu P, Msellati A, Mwipatayi D, Azhar M, Malone A, Fatimi SH, Conway C, Hameed A. Advancements in left ventricular assist devices to prevent pump thrombosis and blood coagulopathy[J]. J Anat, 2023, 242:29-49.

[10] Lee J, Hong SB, Kim YH, Kim HW, Kim DY. Left ventricular assist device implantation combined with hemiarch replacement for severe aortic atherosclerosis[J]. J Thorac Dis, 2023, 15:3979-3983.

[11] Shoskes A, Hassett C, Gedansky A, Starling RC, Estep JD, Tong MZY, Cho SM, Uchino K. Implications of causes of intracranial hemorrhage during left ventricular assist device support[J]. Neurocrit Care, 2022, 37:267-272.

[12] Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson LW, Blume ED, Myers SL, Miller MA, Baldwin JT, Young JB. Seventh INTERMACS annual report: 15, 000 patients and counting[J]. J Heart Lung Transplant, 2015, 34:1495-1504.

[13] Shahreyar M, Bob-Manuel T, Khouzam RN, Bashir MW,

Sulaiman S, Akinseye O, Sharma A, Carter A, Latham S, Bhandari S, Jahangir A. Trends, predictors and outcomes of ischemic stroke and intracranial hemorrhage in patients with a left ventricular assist device[J]. Ann Transl Med, 2018, 6:5.

[14] Molina EJ, Shah P, Kiernan MS, Cornwell WK 3rd, Copeland H, Takeda K, Fernandez FG, Badhwar V, Habib RH, Jacobs JP, Koehl D, Kirklin JK, Pagani FD, Cowger JA. The Society of Thoracic Surgeons Intermacs 2020 annual report[J]. Ann Thorac Surg, 2021, 111:778-792.

[15] Pagani FD, Miller LW, Russell SD, Aaronson KD, John R, Boyle AJ, Conte JV, Bogaev RC, MacGillivray TE, Naka Y, Mancini D, Massey HT, Chen L, Klodell CT, Aranda JM, Moazami N, Ewald GA, Farrar DJ, Frazier OH; HeartMate Ⅱ Investigators. Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device[J]. J Am Coll Cardiol, 2009, 54:312-321.

[16] Slaughter MS, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D, Sun B, Tatooles AJ, Delgado RM 3rd, Long JW, Wozniak TC, Ghumman W, Farrar DJ, Frazier OH; HeartMate Ⅱ Investigators. Advanced heart failure treated with continuous-flow left ventricular assist device[J]. N Engl J Med, 2009, 361:2241-2251.

[17] Rogers JG, Pagani FD, Tatooles AJ, Bhat G, Slaughter MS, Birks EJ, Boyce SW, Najjar SS, Jeevanandam V, Anderson AS, Gregoric ID, Mallidi H, Leadley K, Aaronson KD, Frazier OH, Milano CA. Intrapericardial left ventricular assist device for advanced heart failure[J]. N Engl J Med, 2017, 376:451-460.

[18] Milano CA, Rogers JG, Tatooles AJ, Bhat G, Slaughter MS, Birks EJ, Mokadam NA, Mahr C, Miller JS, Markham DW, Jeevanandam V, Uriel N, Aaronson KD, Vassiliades TA, Pagani FD; ENDURANCE Investigators. HVAD: the ENDURANCE supplemental trial[J]. JACC Heart Fail, 2018, 6:792-802.

[19] Colombo PC, Mehra MR, Goldstein DJ, Estep JD, Salerno C, Jorde UP, Cowger JA, Cleveland JC Jr, Uriel N, Sayer G, Skipper ER, Downey FX, Ono M, Hooker R Jr, Anyanwu AC, Givertz MM, Mahr C, Topuria I, Somo SI, Crandall DL, Horstmanshof DA. Comprehensive analysis of stroke in the long-term cohort of the MOMENTUM 3 study[J]. Circulation, 2019, 139:155-168.

[20] Mehra MR, Uriel N, Naka Y, Cleveland JC Jr, Yuzefpolskaya M, Salerno CT, Walsh MN, Milano CA, Patel CB, Hutchins SW, Ransom J, Ewald GA, Itoh A, Raval NY, Silvestry SC, Cogswell R, John R, Bhimaraj A, Bruckner BA, Lowes BD, Um JY, Jeevanandam V, Sayer G, Mangi AA, Molina EJ, Sheikh F, Aaronson K, Pagani FD, Cotts WG, Tatooles AJ, Babu A, Chomsky D, Katz JN, Tessmann PB, Dean D, Krishnamoorthy A, Chuang J, Topuria I, Sood P, Goldstein DJ; MOMENTUM 3 Investigators. A fully magnetically levitated left ventricular assist device: final report[J]. N Engl J Med, 2019, 380:1618-1627.

[21] Cho SM, Mehaffey JH, Meyers SL, Cantor RS, Starling RC, Kirklin JK, Jacobs JP, Kern J, Uchino K, Yarboro LT. Cerebrovascular events in patients with centrifugal-flow left ventricular assist devices: propensity score-matched analysis from the intermacs registry[J]. Circulation, 2021, 144:763-772.

[22] Kuehn BM. FDA: stop using Medtronic's heartware ventricular assist device[J]. JAMA, 2021, 326:215.

[23] Wang W, Song Y, Zhang YQ, Wang ZQ, Liu ZG, Li SJ, Tang Y, Liu XC. Short-term effect of HeartCon left ventricular assist device on the treatment of 20 adult patients with end-stage heart failure[J]. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue, 2022, 34:1258-1262.[王伟, 宋昱, 张云强, 王正清, 刘志刚, 李树杰, 唐渊, 刘晓程. HeartCon型左心室辅助装置治疗20例成人终末期心衰患者的近期效果观察[J]. 中华危重病急救医学, 2022, 34:1258-1262.]

[24] Liu XC, Wang CS, Zhou XM, Yang B, Chen LW, An Q, Gu TX, Xu ZY, Huang JS, Kong XR, Shao YF. A prospective multicenter clinical trial study of a domestic HeartCon third-generation magnetic and hydrodynamic levitation LVAD for the treatment of 50 cases of end-stage heart failure[J]. Zhonghua Xiong Xin Xue Guan Wai Ke Za Zhi, 2023, 39:273-278.[刘晓程, 王春生, 周新民, 杨斌, 陈良万, 安琪, 谷天祥, 徐志云, 黄劲松, 孔祥荣, 邵永丰. 国产HeartCon第三代磁液悬浮左心室辅助装置治疗50例终末期心力衰竭的前瞻性多中心临床试验研究[J]. 中华胸心血管外科杂志, 2023, 39:273-278.]

[25] Fan TH, Cho SM, Prayson RA, Hassett CE, Starling RC, Uchino K. Cerebral microvascular injury in patients with left ventricular assist device: a neuropathological study[J]. Transl Stroke Res, 2022, 13:257-264.

[26] Cho SM, Floden D, Wallace K, Hiivala N, Joseph S, Teuteberg J, Rogers JG, Pagani FD, Mokadam N, Tirschwell D, Li S, Starling RC, Mahr C, Uchino K. Long-term neurocognitive outcome in patients with continuous flow left ventricular assist device[J]. JACC Heart Fail, 2021, 9:839-851.

[27] Pavol MA, Boehme AK, Willey JZ, Festa JR, Lazar RM, Nakagawa S, Casida J, Yuzefpolskaya M, Colombo PC. Predicting post-LVAD outcome: is there a role for cognition[J]? Int J Artif Organs, 2021, 44:237-242.

[28] Willey JZ, Gavalas MV, Trinh PN, Yuzefpolskaya M, Reshad Garan A, Levin AP, Takeda K, Takayama H, Fried J, Naka Y, Topkara VK, Colombo PC. Outcomes after stroke complicating left ventricular assist device[J]. J Heart Lung Transplant, 2016, 35:1003-1009.

[29] Chatterjee A, Feldmann C, Dogan G, Hanke JS, Ricklefs M, Deniz E, Haverich A, Schmitto JD. Clinical overview of the HVAD: a centrifugal continuous-flow ventricular assist device with magnetic and hydrodynamic bearings including lateral implantation strategies[J]. J Thorac Dis, 2018, 10(Suppl 15):S1785-S1789.

[30] Boyle AJ, Jorde UP, Sun B, Park SJ, Milano CA, Frazier OH, Sundareswaran KS, Farrar DJ, Russell SD; HeartMate Ⅱ Clinical Investigators. Pre-operative risk factors of bleeding and stroke during left ventricular assist device support: an analysis of more than 900 HeartMate Ⅱ outpatients[J]. J Am Coll Cardiol, 2014, 63:880-888.

[31] Acharya D, Loyaga-Rendon R, Morgan CJ, Sands KA, Pamboukian SV, Rajapreyar I, Holman WL, Kirklin JK, Tallaj JA. INTERMACS analysis of stroke during support with continuous-flow left ventricular assist devices: risk factors and outcomes[J]. JACC Heart Fail, 2017, 5:703-711.

[32] Coffin ST, Haglund NA, Davis ME, Xu M, Dunlay SM, Cowger JA, Shah P, Aaronson KD, Pagani FD, Stulak JM, Maltais S; Mechanical Circulatory Support Research Network. Adverse neurologic events in patients bridged with long-term mechanical circulatory support: a device-specific comparative analysis[J]. J Heart Lung Transplant, 2015, 34:1578-1585.

[33] Sherazi S, Goldenberg I, McNitt S, Kutyifa V, Gosev I, Wood K, Chen L, Polonsky B, Vidula H, Alexis JD. Smoking and the risk of stroke in patients with a left ventricular assist device[J]. ASAIO J, 2021, 67:1217-1221.

[34] Stulak JM, Deo S, Schirger J, Aaronson KD, Park SJ, Joyce LD, Daly RC, Pagani FD. Preoperative atrial fibrillation increases risk of thromboembolic events after left ventricular assist device implantation[J]. Ann Thorac Surg, 2013, 96:2161-2167.

[35] Nassif ME, Tibrewala A, Raymer DS, Andruska A, Novak E, Vader JM, Itoh A, Silvestry SC, Ewald GA, LaRue SJ. Systolic

blood pressure on discharge after left ventricular assist device insertion is associated with subsequent stroke[J]. J Heart Lung Transplant, 2015, 34:503-508.

[36] Pinsino A, Castagna F, Zuver AM, Royzman EA, Nasiri M, Stöhr EJ, Cagliostro B, McDonnell B, Cockcroft JR, Garan AR, Topkara VK, Schulze PC, Takeda K, Takayama H, Naka Y, Demmer RT, Willey JZ, Yuzefpolskaya M, Colombo PC. Prognostic implications of serial outpatient blood pressure measurements in patients with an axial continuous-flow left ventricular assist device[J]. J Heart Lung Transplant, 2019, 38: 396-405.

[37] Cowger JA, Shah P, Pagani FD, Grafton G, Stulak J, Chamogeorgakis T, Lanfear D, Nemeh H, Pinney S. Outcomes based on blood pressure in patients on continuous flow left ventricular assist device support: an Interagency Registry for Mechanically Assisted Circulatory Support analysis[J]. J Heart Lung Transplant, 2020, 39:441-453.

[38] Nicholson JD, Kaakeh Y. Pharmacotherapy considerations for long-term management of patients with left ventricular assist devices[J]. Am J Health Syst Pharm, 2018, 75:755-766.

[39] Cho SM, Hassett C, Rice CJ, Starling R, Katzan I, Uchino K. The causes of LVAD-associated ischemic stroke: surgery, pump thrombosis, antithrombotics, and infection[J]. ASAIO J, 2019, 65:775-780.

[40] Inamullah O, Chiang YP, Bishawi M, Weiss M, Lutz MW, Blue LJ, Feng W, Milano CA, Luedke M, Husseini NE. Characteristics of strokes associated with centrifugal flow left ventricular assist devices[J]. Sci Rep, 2021, 11:1645.

[41] Ramey WL, Basken RL, Walter CM, Khalpey Z, Lemole GM Jr, Dumont TM. Intracranial hemorrhage in patients with durable mechanical circulatory support devices: institutional review and proposed treatment algorithm[J]. World Neurosurg, 2017, 108: 826-835.

[42] Uriel N, Pak SW, Jorde UP, Jude B, Susen S, Vincentelli A, Ennezat PV, Cappleman S, Naka Y, Mancini D. Acquired von Willebrand syndrome after continuous-flow mechanical device support contributes to a high prevalence of bleeding during long-term support and at the time of transplantation[J]. J Am Coll Cardiol, 2010, 56:1207-1213.

[43] Crow S, Chen D, Milano C, Thomas W, Joyce L, Piacentino V 3rd, Sharma R, Wu J, Arepally G, Bowles D, Rogers J, Villamizar-Ortiz N. Acquired von Willebrand syndrome in continuous-flow ventricular assist device recipients[J]. Ann Thorac Surg, 2010, 90:1263-1269.

[44] Crow S, Milano C, Joyce L, Chen D, Arepally G, Bowles D, Thomas W, Ortiz NV. Comparative analysis of von Willebrand factor profiles in pulsatile and continuous left ventricular assist device recipients[J]. ASAIO J, 2010, 56:441-445.

[45] Arias K, Sun W, Wang S, Sorensen EN, Feller E, Kaczorowski D, Griffith B, Wu ZJ. Acquired platelet defects are responsible for nonsurgical bleeding in left ventricular assist device recipients[J]. Artif Organs, 2022, 46:2244-2256.

[46] Cho SM, Moazami N, Katz S, Bhimraj A, Shrestha NK, Frontera JA. Stroke risk following infection in patients with continuous-flow left ventricular assist device[J]. Neurocrit Care, 2019, 31: 72-80.

[47] Aggarwal A, Gupta A, Kumar S, Baumblatt JA, Pauwaa S, Gallagher C, Treitman A, Pappas P, Tatooles A, Bhat G. Are blood stream infections associated with an increased risk of hemorrhagic stroke in patients with a left ventricular assist device[J]? ASAIO J, 2012, 58:509-513.

[48] Trachtenberg BH, Cordero-Reyes AM, Aldeiri M, Alvarez P, Bhimaraj A, Ashrith G, Elias B, Suarez EE, Bruckner B, Loebe M, Harris RL, Zhang JY, Torre-Amione G, Estep JD. Persistent blood stream infection in patients supported with a continuous-flow left ventricular assist device is associated with an increased risk of cerebrovascular accidents[J]. J Card Fail, 2015, 21:119-125.

[49] Hasin T, Matsuzawa Y, Guddeti RR, Aoki T, Kwon TG, Schettle S, Lennon RJ, Chokka RG, Lerman A, Kushwaha SS. Attenuation in peripheral endothelial function after continuous flow left ventricular assist device therapy is associated with cardiovascular adverse events[J]. Circ J, 2015, 79:770-777.

[50] Hahn C, Schwartz MA. Mechanotransduction in vascular physiology and atherogenesis[J]. Nat Rev Mol Cell Biol, 2009, 10:53-62.

[51] Agarwal SK, Chambless LE, Ballantyne CM, Astor B, Bertoni AG, Chang PP, Folsom AR, He M, Hoogeveen RC, Ni H, Quibrera PM, Rosamond WD, Russell SD, Shahar E, Heiss G. Prediction of incident heart failure in general practice: the Atherosclerosis Risk in Communities (ARIC) study[J]. Circ Heart Fail, 2012, 5:422-429.

[52] Ben-Shlomo Y, Spears M, Boustred C, May M, Anderson SG, Benjamin EJ, Boutouyrie P, Cameron J, Chen CH, Cruickshank JK, Hwang SJ, Lakatta EG, Laurent S, Maldonado J, Mitchell GF, Najjar SS, Newman AB, Ohishi M, Pannier B, Pereira T, Vasan RS, Shokawa T, Sutton-Tyrell K, Verbeke F, Wang KL, Webb DJ, Willum Hansen T, Zoungas S, McEniery CM, Cockcroft JR, Wilkinson IB. Aortic pulse wave velocity improves cardiovascular event prediction: an individual participant Meta analysis of prospective observational data from 17, 635 subjects[J]. J Am Coll Cardiol, 2014, 63:636-646.

[53] Rosenblum H, Pinsino A, Zuver A, Javaid A, Mondellini G, Ji R, Cockcroft JR, Yuzefpolskaya M, Garan AR, Shames S, Topkara VK, Takayama H, Takeda K, Naka Y, Mcdonnell BJ, Willey JZ, Colombo PC, Stöhr EJ. Increased aortic stiffness is associated with higher rates of stroke, gastrointestinal bleeding and pump thrombosis in patients with a continuous flow left ventricular assist device[J]. J Card Fail, 2021, 27:696-699.

[54] Ibeh C, Tirschwell DL, Mahr C, Creutzfeldt CJ. Medical and surgical management of left ventricular assist device-associated intracranial hemorrhage[J]. J Stroke Cerebrovasc Dis, 2021, 30: 106053.

[55] Frontera JA, Starling R, Cho SM, Nowacki AS, Uchino K, Hussain MS, Mountis M, Moazami N. Risk factors, mortality, and timing of ischemic and hemorrhagic stroke with left ventricular assist devices[J]. J Heart Lung Transplant, 2017, 36:673-683.

[56] Kirklin JK, Naftel DC, Myers SL, Pagani FD, Colombo PC. Quantifying the impact from stroke during support with continuous flow ventricular assist devices: an STS INTERMACS analysis[J]. J Heart Lung Transplant, 2020, 39:782-794.

[57] Morgan JA, Brewer RJ, Nemeh HW, Gerlach B, Lanfear DE, Williams CT, Paone G. Stroke while on long-term left ventricular assist device support: incidence, outcome, and predictors[J]. ASAIO J, 2014, 60:284-289.

[58] Feldman D, Pamboukian SV, Teuteberg JJ, Birks E, Lietz K, Moore SA, Morgan JA, Arabia F, Bauman ME, Buchholz HW, Deng M, Dickstein ML, El-Banayosy A, Elliot T, Goldstein DJ, Grady KL, Jones K, Hryniewicz K, John R, Kaan A, Kusne S, Loebe M, Massicotte MP, Moazami N, Mohacsi P, Mooney M, Nelson T, Pagani F, Perry W, Potapov EV, Eduardo Rame J, Russell SD, Sorensen EN, Sun B, Strueber M, Mangi AA, Petty MG, Rogers J; International Society for Heart and Lung Transplantation. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory

support: executive summary[J]. J Heart Lung Transplant, 2013, 32:157-187.
[59] Gupta G, Yan CL, Kalwar T, Thakkar-Rivera N. Left ventricular assist device thrombosis in the setting of supratherapeutic international normalized ratio (INR) and bleeding[J]. Blood Coagul Fibrinolysis, 2023, 34:414-418.
[60] Sowder A, Ather A, Birks E, Kolodziej A, Malyala R, Sieg A, Schadler A, Unger R, Guglin M, Kuan W. Evaluation of adjusted international normalized ratio goal in patients with HeartMate 3 left ventricular assist devices[J]. Artif Organs, 2023, 47:1613-1621.
[61] Liesdek OCD, Urbanus RT, de Maat S, de Heer LM, Ramjankhan FZ, Sebastian SAE, Huisman A, de Jonge N, Vink A, Fischer K, Maas C, Suyker WJL, Schutgens REG. Insights in the prothrombotic changes after implantation of a left ventricular assist device in patients with end-stage heart failure: a longitudinal observational study[J]. ASAIO J, 2023, 69:438-444.
[62] Martinez J, Smegner K, Tomoda M, Motomura T, Chivukula VK. Encouraging regular aortic valve opening for EVAHEART 2 LVAD support using virtual patient hemodynamic speed modulation analysis[J]. ASAIO J, 2023. [Epub ahead of print]
[63] Nagy P, Sax B, Kozák A, Merkely B, Osztheimer I, Jobbágy Á. Automatic non-invasive blood pressure measurement in left ventricular assist device patients with a photoplethysmography assisted device[J]. Int J Artif Organs, 2023, 46:274-279.
[64] Rowe S, Green S, Albrecht B, Pouch SM. Long-term dalbavancin for suppression of gram-positive chronic left ventricular assist device infections[J]. Open Forum Infect Dis, 2023, 10:ofad537.
[65] Schmalz G, Hennecke A, Haak R, Kottmann T, Garbade J, Binner C, Ziebolz D. Secondary analysis of potential associations between oral health and infection-related parameters in patients with severe heart failure: results of a German cohort[J]. BMC Cardiovasc Disord, 2023, 23:573.

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·读者·作者·编者·

《中国现代神经疾病杂志》编辑部关于稿件参考文献的要求

《中国现代神经疾病杂志》编辑部对来稿的参考文献一律按照GB/T 7714-2005《文后参考文献著录规则》采用顺序编码制著录，依照其在文中出现的先后顺序用阿拉伯数字加方括号标出。尽量避免引用摘要作为参考文献。内部刊物、未发表资料、个人通信等请勿作为文献引用。每条参考文献著录项目应齐全，不得用“同上”或“ibid”表示。参考文献中的主要责任者（专著作者、论文集主编、学位申报人、专利申请人、报告撰写人、期刊文章作者、析出文章作者）均全部列出。外文期刊名称用缩写，以*Index Medicus*中的格式为准，中文期刊用全名。每条参考文献均须著录起止页码。中英文双语形式著录时，文献序号后先列出完整的中文文献英译文，再列出中文文献。作者姓名的英译文采用汉语拼音形式表示，姓大写，名用缩写形式，取每个字的首字母，大写。期刊名称以汉语拼音注录。

（1）期刊著录格式：主要责任者. 题名[文献类型标志/文献载体标志]. 刊名, 年, 卷:起页-止页.

举例：[1]Gao S. Ten-year advance of transcranial Doppler ultrasonography[J]. Zhongguo Xian Dai Shen Jing Ji Bing Za Zhi, 2010, 10:127-136.[高山. 经颅多普勒超声十年进展[J]. 中国现代神经疾病杂志, 2010, 10:127-136.]

（2）著作或编著著录格式：主要责任者. 题名: 其他题名信息[文献类型标志/文献载体标志]. 其他责任者（例如翻译者）. 版本项（第1版不著录）. 出版地: 出版者, 出版年: 引文起页-止页.

举例：[2]Louis DN, Ohgaki H, Wiestler OD, Cavenee WK. WHO classification of tumours of the central nervous system[M]. 4th ed. Li Q, Xu QZ, Trans. Beijing: Editorial Office of Chinese Journal of Diagnostic Pathology, 2011: 249-252.[Louis DN, Ohgaki H, Wiestler OD, Cavenee WK. 中枢神经系统肿瘤WHO分类[M]. 4版. 李青, 徐庆中, 译. 北京: 诊断病理学杂志社, 2011: 249-252.]

（3）析出文献著录格式：析出文献主要责任者. 析出文献题名[文献类型标志/文献载体标志]//专著主要责任者. 专著题名: 其他题名信息. 版本项（第1版不著录）. 出版地: 出版者, 出版年: 析出文献起页-止页.

举例：[3]吕传真. 肌肉疾病[M]//史玉泉. 实用神经病学. 3版. 上海: 上海科学技术出版社, 1994: 564-576.

（4）电子文献著录格式：必须于题名后著录[文献类型标志/文献载体标志]，一般同时于起页-止页后著录[引用日期]以及获取和访问路径.

举例：[4]Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role[J/OL]. Am J Nurs, 2002, 102(6):23[2002-08-12]. http://www.nursingword.org/AJN/2002/june/Wawatch.htm.

[5]Foley KM, Gelband H. Improving palliative care for cancer[M/OL]. Washington: National Academy Press, 2001 [2002-07-09]. http://www.nap.edu/books/0309074029/html.

（5）会议文献著录格式：主要责任者. 题名: 其他题名信息[文献类型标志/文献载体标志], 会议地点, 年份. 出版地: 出版者, 出版年: 引文起页-止页.

举例：[6]中国科技期刊编辑学会医学分会, 中华医学会杂志社. 第一届全国医药卫生期刊管理和学术研讨会资料汇编[C], 北戴河, 2002. 北京: 中国科技期刊编辑学会医学分会, 2002.