心房颤动与认知功能障碍

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【摘要】 心房颤动(房颤)可影响认知功能。房颤导致血栓形成及脱落造成脑卒中，可影响认知功能。近年有研究证明，房颤还可能通过大脑低灌注、血管内皮功能异常、无症状性脑梗死、脑白质损害及大脑微出血、血管周围间隙扩大等机制影响认知功能。治疗房颤的抗凝药物、射频消融术也可影响患者的认知功能。

【关键词】 心房颤动；认知；无症状性脑梗死；抗凝；射频消融术
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心房颤动(房颤)是临床常见的心律失常，其人群发病率约为 1%，房颤患者可出现认知障碍，两者之间的关系受到越来越多的关注[1]。认知功能障碍是指由各种原因导致的不同程度的认知功能损害，程度从轻度认知功能障碍到重度痴呆。痴呆是认知功能障碍最严重程度，以认知功能及独立能力不可逆性丧失为特征，常发生在老年人群中。据统计，在 60 岁以上的老年人群中，痴呆的发生率大约 5%～7%，随着老年人口的增多，痴呆的发生率也会增加[2]。

与正常窦性心率相比，房颤致认知功能下降的风险可增加 2～3 倍。Bunch 等[3]对房颤患者进行连续 5 年的随访发现，房颤是认知功能障碍的独立危险因素，且房颤患者可出现老年性痴呆、血管性痴呆及阿尔兹海默病等各种痴呆类型。除脑卒中房颤患者的认知功能下降外，非卒中房颤患者也可出现认知评分下降[4-5]。

1　房颤导致认知功能障碍

1.1　房颤所致血栓形成与认知功能

房颤是脑卒中发生的独立危险因素。房颤患者存在左心耳心内膜的结构改变、左心房扩张致血液瘀滞、血液中促凝成分的异常增多等，可致左心房内形成血栓并脱落，导致脑卒中。房颤导致的急性脑卒中事件占所有脑卒中病因的 1/3。脑卒中可迅速降低认知评分，并可导致长期认知障碍[6]。目前房颤患者主要用 CHA2DS2-VASc 评分来评估血栓形成风险，评分＞2 分的房颤患者有较高的血栓形成风险，需要应用抗凝药物治疗。但也有研究认为 ATRIA 评分较 CHA2DS2-VASc 更有利于预测评估房颤患者形成血栓的风险[7-8]。

1.2　房颤所致大脑低灌注与认知功能

房颤患者心房收缩不同步、心室频率及节律异常均可导致心输出量下降。房颤患者的心室率控制过慢或过快均可导致认知功能损害或者痴呆[9]。房颤患者存在脑血流灌注不足情况，在阵发性及持续性房颤中均可观察到此现象，且随着房颤率的增快大脑平均血流速度亦减慢[10-11]。研究发现在难治性房颤患者中，大脑前额叶及后顶叶区域性脑血流可减少 14%～21%，与对照组相比，房颤组患者的认知功能明显下降[11]。

长期大脑低灌注可导致神经细胞葡萄糖及能量供应不足，进一步可导致神经细胞功能障碍甚至神经细胞死亡，而这种过程易发生在对化学变化敏感的区域，如海马区及特定大脑皮层区域等[12]。

1.3　房颤所致无症状性脑梗死与认知功能

无症状性脑梗死是一种无临床相关症状但影像学检查发现有脑梗死灶的系列统称，也称为亚临床微栓塞。房颤患者发生无症状性微栓塞的概率是非房颤患者的 2～3 倍，且可引起认知功能减退，微栓子所在的区域比微栓子的数量及密度更重要[13-14]。无症状性微栓塞还可促进全脑萎缩及脑室扩大，进一步损害认知功能[15]。房颤患者微栓子的形成机制目前尚不清楚。

另外，在房颤患者中亦发现存在脑白质损害，

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表现为室周、脑深部及皮层下白质高信号。房颤患者的皮层或皮层下及脑深部区域存在更多的微栓塞[16]。脑白质损害和微栓子均可导致认知功能的损害，脑白质损害更容易引起广泛的认知减退，而微栓子可能更容易造成额叶功能受损[14]。

1.4 房颤所致血管内皮功能异常与认知功能

房颤患者不仅存在心内膜内皮损伤，全身外周血管功能亦存在异常变化，如外周血管舒张功能受损[17]。房颤患者的内皮损伤不仅可致血管功能异常，还可导致促炎性因子及促血栓因子的释放，如血管性血友病因子(vWF)、黏附因子、E 选择素、微粒、白细胞介素-6(IL-6)、肿瘤坏死因子-α(TNF-α)、单核细胞趋化蛋白-1(MCP-1)、血管内皮生长因子(VEGF)等[18]。而这些因子的升高不仅可导致血栓前状态，促进血栓形成，而且与阿尔兹海默病及血管性痴呆的发生均有相关性[19]。C 反应蛋白也与房颤相关，高水平的 C 反应蛋白与认知功能障碍的风险增加相关[20-21]。此外，内皮损害可能会引起脑微出血灶的发生[22]，引起认知损害。

1.5 房颤所致脑微出血与认知功能

脑微出血是由脑小血管损伤造成，房颤患者发生脑微出血的概率较高[22]。治疗房颤使用的抗凝药可以减少脑卒中的发生，但同时也增加了脑出血的风险。1 项大型横断面研究发现，在服用香豆素类药物的人群中，脑微出血的发生率达 19.4%，在服用香豆素类药物平均 3.9 年后，脑微出血的发生率达 6.9%。香豆素类抗凝药使脑微出血的发生率增高，且脑微出血的发生与凝血酶原时间国际标准化比值(INR)的增高及不稳定有关[23]。脑微出血灶可以引起认知障碍，微出血灶的数量越多，认知障碍越严重[24]。

1.6 房颤所致血管周围间隙扩大与认知功能

房颤患者血清中 N 末端脑钠肽前体(N-proBNP)水平增高，可致血管周围间隙扩大等脑小血管病[25-26]。有研究发现血管周围间隙扩大可导致认知障碍[27]，与脑白质损伤也具有相关性[28]。

2 房颤相关治疗与认知功能障碍

2.1 抗凝药物

使用抗凝药物可减少 80%的脑卒中发生[29]，可减少总体房颤患者认知下降的比例。然而，抗凝药物并不能防止房颤患者认知功能的下降[30]。在与阿司匹林对照的一项研究中，没有发现华法林对非卒中性房颤患者的认知功能受损有预防作用[31]。有研究发现，长期使用阿司匹林可以降低阿尔兹海默病的发生[32]。房颤患者的认知障碍与华法林的使用时间长短相关，长期应用维持量华法林可减少认知障碍的发生[33]。

目前，对年龄＜65 岁、CHA2DS2-VASc 评分为 0的房颤患者并不推荐使用抗凝药物[34]。但在未使用抗凝药物的房颤人群中，无症状性脑微栓塞发生率很高，如果抗凝药物可预防认知功能的下降，那么这部分患者是否需要接受抗凝治疗则需进一步的研究。

2.2 经导管射频消融术

经导管射频消融术已成为治疗房颤的一线治疗。有研究发现，射频消融术后可能发生无症状性脑栓塞，但大部分无症状性脑栓塞在数月后可自行消失，没有发现射频消融术所致的无症状性脑栓塞与认知相关[35]。

经导管射频消融术后，无症状脑栓塞的发生机制尚不清楚，可能与微气泡及大量微血栓碎片形成的混合物有关。Efimova 等[11]在对房颤患者进行射频消融及安装起搏器后，行脑血流评估，表明脑血流灌注有很大改善，右额区域血流可增加 11.5%，患者整体认知功能也有改善。

2.3 抗炎治疗

抗炎还不是房颤的常规治疗。有研究表明应用阿托伐他汀强化治疗可以降低房颤患者血浆 C 反应蛋白及其他炎性因子水平[36]。而炎性因子的减少可改善房颤患者认知功能，尤其在记忆和信息处理速度方面改善明显[37]。

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