· 综述 ·

Progresses of percutaneous intramyocardial septal radiofrequency ablation of hypertrophic obstructive cardiomyopathy

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[**Abstract**] Hypertrophic obstructive cardiomyopathy (HOCM) is characterized by dynamic obstruction of the left ventricular outflow tract, which may cause sudden cardiac death. Early intervention is essential to improve prognosis. Percutaneous intramyocardial septal radiofrequency ablation (PIMSRA) provided a new option for septal reduction of HOCM. The progresses of PIMSRA for treating HOCM were reviewed in this paper.

[**Keywords**] cardiomyopathy, hypertrophic; ventricular septum; electrocoagulation; echocardiography
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经皮心肌内室间隔射频消融治疗肥厚型梗阻性心肌病进展

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[**摘　要**] 肥厚型梗阻性心肌病(HOCM)以左心室流出道动态性梗阻为特征, 可引起心源性猝死; 早期干预对于改善预后至关重要。经皮心肌内室间隔射频消融(PIMSRA)为室间隔减容治疗HOCM提供了新的选择。本文围绕PIMSRA治疗HOCM进行综述。

[**关键词**] 心肌病, 肥厚型; 室间隔; 电凝术; 超声心动描记术
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对于肥厚型梗阻性心肌病(hypertrophic obstructive cardiomyopathy, HOCM), 以负性肌力药物治疗的有效率不足50%[1-2]。肌球蛋白抑制剂Mavacamten可减轻左心室流出道梗阻、改善左心室舒张功能[3-5], 但不适用于严重HOCM。通过室间隔减容治疗HOCM的有效性已得到临床验证; 经皮心肌内室间隔射频消融(percutaneous intramyocardial septal radiofrequency ablation, PIMSRA)为此提供了新的可选方案。本文就PIMSRA治疗HOCM进展进行综述。

1　HOCM病理生理机制

肥厚型心肌病(hypertrophic cardiomyopathy, HCM)是最常见的遗传性心肌疾病之一, 为编码心肌肌节相关蛋白基因发生致病性变异所致[6]。心肌肌节松弛时, 肌球蛋白构象可呈超松弛或无序松弛状态, 其比例可影响心肌收缩力和能量利用, 在正常情况下有助于维持心肌工作和代谢的平衡[7]; HCM致病性错义突变可使该比例失衡而致心肌发生收缩异常及形态重塑等改变。

HCM常见解剖学改变为左心室非对称性肥厚伴二尖瓣功能异常; 前者可使左心室血流方向改变, 后者可表现为收缩期二尖瓣前向运动; 严重HCM患者心室收缩时血液将二尖瓣叶推入左心室流出道而致左心

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室流出道动态性梗阻[8-10]；静息态左心室流出道压力梯度超过30 mmHg或负荷态超过50 mmHg则为HOCM，解除梗阻及缓解症状为外科手术或介入治疗HOCM的目标。

2　PIMSRA治疗HOCM

治疗HOCM的传统方法包括室间隔切除术（septal myectomy，SM）及酒精室间隔消融（alcohol septal ablation，ASA），均为治疗药物难治性HOCM的常用方式[10-11]。SM术后左心室流出道压力梯度降低，可有效缓解HOCM患者运动不耐受等症状。SM可促进心肌逆向重塑[12-13]。超声二维斑点追踪成像（two-dimensional speckle tracking imaging，2D-STI）应变参数可定量描述心肌形变；HOCM左心室整体纵向应变（global longitudinal strain，GLS）受损与心源性猝死、心力衰竭等不良预后有关[14-15]。另有研究[16]报道SM术后1年HOCM患者左心房容积显著减少，有利于缓解左心房力学功能障碍；但同时左心室GLS缩小，导致左心室心肌力学功能障碍进展，提示SM或未能对左心室心肌力学产生积极影响。此外，SM术中需开胸并进行体外循环，部分患者可能难以耐受。ASA为可替代SM治疗药物难治性HOCM左心室流出道梗阻的介入方法，但对冠状动脉间隔支存在解剖变异具有较强依赖性，且可致三度房室传导阻滞等严重并发症，约10%HOCM患者于ASA后需要植入永久性起搏器[17]。

PIMSRA则是在经胸超声心动图（transthoracic echocardiogram，TTE）引导下经皮入路于心尖部进针，沿室间隔长轴将电极针刺入肥大的室间隔前部，通过射频消融使局部心肌发生凝固坏死，使室间隔局部萎缩、变薄而获得减容效果[18-20]。

2.1　PIMSRA的可行性与安全性　PIMSRA治疗HOCM临床效果确切，中长期随访结果显示预后改善，提示其具有良好可行性及安全性，但可能出现心包积液等并发症，故应采取个体化策略，选取最佳进针位点及路径，并在治疗后常规行TTE，观察有无心包压塞等严重并发症。

LIU等[20]采用经皮心肌内入路以PIMSRA治疗15例HOCM，由于避开了心内膜及其下方神经传导系统，治疗后未见束支传导阻滞或完全性房室传导阻滞，患者长期预后获得改善；1例因冠状动脉损伤而出现心包压塞。ZHOU等[21]对200例接受PIMSRA治疗HOCM患者进行随访，中期结果显示PIMSRA疗效良好，并发症发生率较低，且可通过操作前CT血管造影及操作时CDFI明确最佳进针位点及路径而降低冠状动脉损伤引发心包压塞的风险。另有个案报道[22]提示可利用钢丝圈栓塞治疗PIMSRA损伤室间隔冠状动脉所致血肿。

针对27例接受PIMSRA的HOCM患者的随访研究[23]结果显示，治疗过程中无死亡病例；治疗后2例发生心包积液并发展为心包压塞而接受开胸手术，1例发生心室颤动但经电复律治疗而复苏；治疗后1年1例死于外伤，26例在5年随访期间纽约心脏协会分级改善，左心室流出道梯度降低、室间隔厚度及左心室后壁厚度变薄，基于心脏MRI测得左心室质量指数及左心室容积指数下降，左心室GLS改善，提示PIMSRA具有改善HOCM远期症状与血流动力学的潜力。

HOCM合并主动脉瓣狭窄时无法经主动脉入路行室间隔减容；PIMSRA对此具有独特优势。LIU等[24]以PIMSRA治疗1例主动脉瓣机械瓣置换后HOCM，LI等[25]则采用经导管主动脉瓣置换与PIMSRA治疗1例主动脉瓣狭窄合并HOCM患者，均获得良好效果。

室间隔血供丰富多变，约20% HOCM患者于ASA后需接受再次干预[9]。XU等[26]以PIMSRA治疗1例ASA后严重残余左心室流出道梗阻HOCM，治疗后压力梯度下降且未出现相关并发症，提示PIMSRA可作为对经ASA失败HOCM患者进行再次干预的备选方案。SHU等[27]以PIMSRA再干预1例ASA治疗失败HOCM，PIMSRA后2 h患者出现左心室流出道梗阻并致心源性休克及左心室射血分数显著下降，经静脉-动脉体外膜肺氧合（extracorporeal membrane oxygenation，ECMO）治疗后恢复窦性心律且血压稳定，但撤除ECMO后约10 h患者出现心包压塞，引流出190 ml血性心包积液后症状改善；可能与射频消融引发组织水肿及穿刺出血有关。此外，PIMSRA后QRS波幅下降与治疗后左心室肥厚消退有关，提示后者可作为评估PIMSRA后室间隔重塑的指标[28]。

2.2　PIMSRA后心肌力学变化　通常以室间隔厚度、左心室流出道压力梯度水平等指标评估PIMSRA治疗HOCM效果，而关于PIMSRA对心肌潜在力学功能的影响目前鲜有报道。

2D-STI能敏感地显示潜在亚临床心功能改变[29]、检测左心室舒张及收缩功能障碍[30-31]；2D-STI GLS等应变参数不似组织多普勒成像技术受角度依赖等限制，可量化全局和局部心肌运动，为评价PIMSRA治

疗HOCM效果的有力指标[16,32]。通过2D-STI还可获得左心房应变参数，包括储存期应变、管道期应变和收缩期应变[33]。DAI等[34]观察PIMSRA后HOCM患者左心房功能变化，发现其储存期及管道期应变明显增高，而收缩期应变并无改善，提示PIMSRA可有效改善左心房储存和导管功能，但短期内收缩功能并无明显改善。存储期应变减低可致左心室舒张功能障碍及心房颤动；PIMSRA后HOCM患者储存期应变增高进一步显示其对HOCM远期预后具有有益影响。

LI等[35]采用超声三维斑点追踪成像（three-dimensional speckle tracking imaging，3D-STI），以左心室GLS、径向应变（radial strain，RS）及周向应变（circumferential strain，CS）等参数全面评估HOCM患者PIMSRA前、治疗后即刻及治疗后1年左心室心肌力学变化，结果显示治疗后即刻室间隔消融节段RS和CS显著降低而GLS无明显变化，治疗后1年左心室GLS显著改善，所获短期结果与QIAN等[32]不符但长期结果与之类似，且治疗后1年室间隔消融节段RS和CS亦恢复。不同方向心肌纤维协同使左心室以复杂而有效的方式收缩，其中，心肌中层纤维围绕短轴呈圆形排列，其收缩导致心肌径向和周向缩短，而内层（心内膜下方）心肌则分布高密度纵向纤维[36-37]，上述差异有助于理解治疗后即刻3D-STI表现，即PIMSRA消融部位在心肌中层而避开心肌内层，故GLS未受损而RS及CS减低；治疗后随室间隔变薄及左心室流出道梗阻解除，消融部位周围组织恢复、微循环改善，使RS和CS逐渐恢复正常。

GLS受损与HOCM患者心血管不良事件风险增加有关[14-15]。PIMSRA治疗后1年GLS显著改善，提示其治疗HOCM改善长期预后优于SM及ASA。

3　相关研发进展

常规临床检查无法确诊HOCM时，需行心肌活检。HAN等[38]在以PIMSRA治疗HOCM的基础上开发了Liwen心肌活检（Liwen myocardial biopsy，LMB）技术，即在TTE引导下进针到位，对17例患者于射频消融前先行心肌活检，以获取心肌组织样本，取材成功率为100%，仅1例发生心包积液，未见心律失常及传导异常，表明其可行性及安全性均良好。

常规PIMSRA所用Cool-tip系统射频针电极不能完全匹配预期消融范围。不同于肿瘤消融强调“尽可能消融肿瘤及邻近组织”，“适形消融”用于治疗HOCM时，需严格控制消融范围在室间隔内，以避免引发穿孔，同时保证消融边界与心内膜之间的安全距离，从而保护传导系统。WANG等[39]对PIMSRA进行系统性调整与升级而研发了Liwen Liu射频消融系统，经优化电极可更精确地控制消融范围而实现“适形消融”，其无级消融电极长度可调，可通过调整电极曝光长度而对室间隔不同部位实现充分、准确消融，疗效及预后与常规PIMSRA相当而安全性更佳。

4　小结

PIMSRA为室间隔减容治疗HOCM提供了新的选择，可能成为治疗HOCM的重要手段，但仍存在局限性，且需致力于减少心包压塞等严重并发症。尽管以PIMSRA治疗HOCM左心室流出道梗阻已实现标准化，但现有研究多为单中心设计，未来需开展大规模、多中心临床研究进一步观察；以超声无创评估心肌做功技术观察PIMSRA治疗HOCM后心肌力学及功能改变，并与超声应变参数进行对比，同时探索将PIMSRA用于治疗心脏肿瘤等。

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