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慢性心力衰竭患者应用高强度间歇性有氧训练研究进展

戴玫¹ 付珞² 胡建英¹ 综述 唐炯¹ 审校

(1. 成都市第三人民医院心血管病研究所, 四川 成都 610031; 2. 成都市第三人民医院康复医学科, 四川 成都 610031)

【摘要】 高强度间歇性有氧训练能改善慢性心力衰竭患者的心肺储备功能、提高运动耐力, 改善内皮功能、逆转左室重构, 提高生活质量, 对左室射血分数保留的心力衰竭、老年和女性患者同样安全有效, 但是目前均是样本量较小的实验性研究, 尚需多中心随机研究以及长期系统的回顾性和总结性研究成果来证实。

【关键词】 慢性心力衰竭; 高强度间歇性有氧训练; 预防; 治疗

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Advances in Research on High-intensity Interval Training in Chronic Heart Failure

DAI Mei, FU Luo, HU Jianying, TANG Jiong

(1. Cardiovascular Disease Research Institute, The Third People's Hospital of Chengdu, Chengdu 610031, Sichuan, China; 2. Department of Rehabilitation Medicine, The Third People's Hospital of Chengdu, Chengdu 610031, Sichuan, China)

【Abstract】 High-intensity interval training have positive effects on chronic heart failure with regard to reversal of cardiac remodeling, aerobic capacity, endothelial function, and quality of life, even in elderly and female patients with chronic heart failure, as well as on heart failure with preserved ejection fraction. Based on pilot studies, these results need to be verified by some randomized multi-center studies and systemic long-term retrospective cohort analysis.

【Key words】 Chronic heart failure; High-intensity interval training; Prevention; Treatment

据统计, 全球慢性心力衰竭 (chronic heart failure, CHF) 患者达 2 250 万, 并且每年新增病例数 200 万, 中国心血管健康多中心合作研究抽样调查 35~74 岁城乡居民 15 518 人, 心力衰竭患病率为 0.9%; 随着年龄增长, 心力衰竭的患病率显著上升^[1]。尽管如 β 受体阻滞剂、血管紧张素转换酶抑制剂 (angiotensin converting enzyme inhibitors, ACEI)、醛固酮受体拮抗剂等药物的规范化使用和器械治疗的进展, 心力衰竭仍是目前死亡的主要原因, CHF 正在成为世界心血管领域的重要公共卫生学问题。

许多临床研究发现遵循个体化方案的体育锻炼 (physical activity) 和运动训练方案对 CHF 患者是安全有效的, 能改善心力衰竭患者的临床症状、运动耐力并延长预期寿命^[2-7]。其机制包括: 控制心血管危险因素, 改善左心室收缩舒张功能、肺脏和骨骼肌功能、内皮功能等^[8]。因此, 国内外指南和共识均把规律性体育锻炼和运动训练作为 CHF 规范化管理的一个重要部分。现有数据显示与中强度运动 (moderate continuous training, MCT) 比较, CHF 患者更能适应高强度间歇性有氧训练 (high-intensity interval training,

HIT)^[9-10]。现就 HIT 在 CHF 患者中的应用进展进行综述。

1 HIT

HIT 是指多组高强度运动训练之间以低强度运动训练间歇进行或以完全休息形成间歇期^[11]。相对于心血管病患者而言,郭兰等^[12]定义 HIT:进行 3~6 组、每组 2~5 min 高强度运动训练,强度以 75%~90% 峰值摄氧量(peak oxygen uptake, VO_{2peak})为标准,在每两组高强度训练之间以较低强度的运动(50%~70% VO_{2peak})或完全休息形成间歇期。HIT 的特点在于运动强度达到最大或接近最大的运动能力,但高强度运动时间相对较短,并可通过间歇期避免不适症状的出现,所以更容易被接受及完成。

Reindell 和 Roskamm 提出“间歇训练”的概念,并证实 HIT 能改善运动耐力、提高运动员成绩^[13]。学者们认为,中央(心血管)和外周(骨骼肌)的良好适应是有氧能力提高的原因^[14-15]。出于安全性考虑,HIT 多用于运动员,近年研究证实,CHF 患者进行 HIT 康复并无不良反应。如在 Koufaki 等^[16]的研究中,纳入存在心力衰竭症状且射血分数<45%的窦性心律患者,平均年龄 59.1 岁,随机分为 HIT 组($n=8$)和 MCT 组($n=9$)训练 6 个月,结果发现相比 MCT,CHF 患者对 HIT 有良好的适应性,在 CHF 患者中实施 HIT 是可行的。

2 HIT 对 CHF 患者的影响

2.1 改善 CHF 患者心肺储备功能

Wisløff 等^[17]进行一项随机研究,纳入 27 例心肌梗死后稳定心力衰竭患者[年龄(75.5 ± 11.1)岁,射血分数 29%, VO_{2peak} 13 mL/(kg·min)],规范化药物治疗基础上随机分入 HIT 组(每次训练 4 组,每组训练持续时间 4 min 高强度运动,达到 90%~95% 峰值心率,继之 3 min 低强度运动恢复期,每次运动前后均有 5~10 min 热身运动和整理运动,每周 3 次)和 MCT 组(运动强度达 70% 峰值心率),共 12~16 周运动训练。结果显示 HIT 组较 MCT 组 VO_{2peak} 升高(46% vs 14%, $P \leq 0.001$),提示运动耐力明显改善。另两项纳入冠状动脉疾病患者的研究显示,患者每周 3~5 次有氧间歇运动训练,训练强度为 50%~95% VO_{2peak} ,12 个月后 VO_{2peak} 增加 37%~42%^[18-19]。但 Pouleur 等^[20]的研究发现 HIT 组和 MCT 组 VO_{2peak} 均较基线时增加,通气阈增加,步行速度改善,两组间无明显差异,提示 HIT 比 MCT 在 CHF 并没有更多获益。现有的临床研究均是单中心、纳入人数较少的研究,尚需更大规模、更高质量的多中心研究证实。

2.2 改善 CHF 患者心脏功能,逆转左室重构

心力衰竭大鼠模型显示强度达到 90% VO_{2peak} 有氧间歇训练能改善受损心肌细胞的收缩功能,减少心肌肥厚,降低血清心房脑钠肽水平。Yu 等^[21]的研究显示与心脏再同步化治疗 3 个月后相似,HIT 分别降低左室舒张末期容积 18% 和收缩末期容积 25%。既往的研究证实 ACEI 能延缓心力衰竭进程,CHF 患者联合 ACEI 和 β 受体阻滞剂治疗能提高射血分数 12%^[22],CHF 患者采用 HIT 训练得到相似的结论。研究显示在药物治疗基础上加用 HIT 可能会获得更强的逆转重构的功效,而且射血分数、每搏量、二尖瓣环运动、由组织多普勒成像测定的二尖瓣环收缩期速度等心肌收缩功能指标得到明显改善,HIT 组左室舒张末期直径和收缩末期直径分别降低 12%、15%,左室舒张末期容积和收缩末期容积分别降低 18%、25%;评判心力衰竭预后和严重程度的指标 B 型脑钠肽前体降低 40%^[17]。这一结果与既往的研究结果血管紧张素 II 受体拮抗剂氯沙坦改善心脏重构和心肌功能相一致。因此,HIT 可以作为心肌梗死后心力衰竭患者的有效康复训练方式。HIT 对心力衰竭患者左室重构的对照研究(Controlled study of myocardial recovery after interval training in heart failure The SMARTEX-HF)^[23]是一项由欧洲 7 个中心共同参与的多中心研究,评估 HIT、MCT 及体育锻炼 3 种不同的运动训练强度和模式对 CHF 患者左室重构的影响,这是由欧洲心血管预防和康复委员会支持正在进行的研究,期待这一大规模研究能成为心力衰竭患者运动训练领域的一个新突破。

2.3 改善 CHF 患者内皮功能、神经内分泌环境

内皮功能不全会导致 CHF 患者运动耐受不良、心肌灌注受损、左室重构,是心血管事件的独立预测因子^[24]。正如 Linke 等^[25]研究显示运动训练对 CHF 患者骨骼肌产生抗氧化效果。HIT 较 MCT 增加抗氧化状态 15% ($P=0.02$),改善内皮功能介导的血管扩张($R=0.67$, $P<0.01$),可能是因为 HIT 增加一氧化氮的生物利用度,降低氧化应激,提高抗氧化状态。HIT 比 MCT 更有效的原因尚不可知,但是推测可能与 HIT 患者具有更高对切应力促发细胞水平甚或分子水平的机制有关。尽管研究显示 HIT 改善一氧化氮介导的内皮功能,但是运动训练组没有发现内皮素-1 和胰岛素样生长因子-1 的改变,可能提示耐力训练通过其他途径改善内皮功能^[17]。

2.4 改善 CHF 患者生活质量

Wisløff 等^[17,26]研究显示 HIT 改善 CHF 患者生活质量,其机制目前尚不清楚,可能与高强度运动增加

患者的机体适应性和运动能力有关。也有报道 HIT 改善 CHF 患者的焦虑抑郁状态。

3 HIT 对特殊人群的影响

3.1 HIT 对左室射血分数保留心力衰竭患者的影响

射血分数保留的心力衰竭 (heart failure with preserved ejection fraction, HF-PEF) 患者可占到心力衰竭人群的 50%^[27], HF-PEF 首次发病后 5 年生存率为 43%, 总体病死率可能与射血分数降低心力衰竭 (heart failure with reduced ejection fraction, HF-REF) 患者的病死率相当^[28]。HF-PEF 的临床研究 (PEP-CHF、CHARM-Preserved、I-Preserve、J-DHF 等) 均未能证实对 HF-REF 有效的药物如 ACEI、血管紧张素 II 受体拮抗剂、 β 受体阻滞剂等可改善 HF-PEF 患者的预后和降低病死率^[29]。现有小样本临床试验和数据报道^[30-34] 有氧耐力运动训练可以提高 VO_{2peak} , 增加运动耐量, 逆转心房重构, 改善左心室舒张功能, 改善生活质量。但是仍需大规模随机对照临床研究结果评判 HF-PEF 患者最适合的运动训练模式。预防和治疗舒张性心力衰竭患者的优化运动训练模式研究 (the optimising exercise training in prevention and treatment of diastolic heart failure study, OptiEx-CLIN)^[35] 是一项前瞻性随机对照多中心研究, 旨在研究 HF-REF 患者适合的运动训练剂量。拟纳入 180 例稳定 HF-PEF 患者, 随机 (1:1:1) 分为 MCT、HIT 和对照组, 纳入者最初 3 个月在严密的医学监控下进行训练, 继之在远程医疗监控下进行 9 个月训练, 研究要求观察患者的运动能力改变情况, 以及舒张功能、内皮功能、生物学标志物、生活治疗的改变情况。这项研究于 2014 年 7 月开始纳入病例, 初步研究结果将于 2017 年发布。

3.2 HIT 对老年 CHF 患者的影响

老年患者心力衰竭患病率随年龄增加而增加, 有 88% 和 49% 的患者分别在 65 岁和 80 岁首次诊断心力衰竭^[36]。老年 CHF 患者是否需要特殊的训练模式引起越来越多的争论。但是, 大量的临床研究均未报道不同年龄患者采用功率车、跑台或是阻力训练会引起严重的不良反应^[37-39]。Wisloff 等^[17] 研究显示 HIT 对老年 CHF 患者和心血管功能严重受损的患者是可行的。莱比锡老年心力衰竭患者运动训练干预研究 (Leipzig Exercise Intervention in CHF and Aging Study, LEICA)^[40] 显示 55 岁和 65 岁的老年 CHF 患者 4 周强化有氧耐力训练 (每次训练 4 组, 训练总时间 20 min, 每周 5 次) 后 VO_{2peak} 分别升高 26%、27%。

3.3 HIT 对女性 CHF 患者的影响

临床研究中, 女性以运动为基础的心脏康复参与

率低于男性^[41]。由于医生和家庭支持有限, CHF 患者合并症多、骨骼肌系统疾病并存等因素是女性参与度低的主要原因^[42-44]。但是女性在结构化运动训练项目中的低参与率是一个严峻的现实, 女性本就比男性基础心功能差, 因此有更高的残疾风险。与男性相同程度的通气功能和健康状况比较, 女性由于肌肉质量偏低, VO_{2peak} 和 6 分钟步行距离明显低于男性。另一方面, 参与运动训练的女性 CHF 患者可以得到与男性相当程度的运动能力的提高, 骨骼肌糖氧化分解酶活性的升高和生活质量的改善^[42]。所以强烈推荐女性 CHF 患者参加以结构化运动训练为基础的康复训练项目。

4 小结

CHF 是一组复杂的临床综合征, 是各种心脏疾病的严重和终末阶段。大量研究证实, 对 CHF 患者进行 HIT 是安全、有效的, HIT 能改善其运动耐量和心功能和内皮功能, 提高生活质量。因此, 尚需进一步探索和制定科学有效的运动训练强度和训练模式是心力衰竭治疗领域未来的研究方向及新突破。

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