

doi: 10.13241/j.cnki.pmb.2018.11.025

有氧康复运动对慢性心力衰竭患者心室重构及血管内皮功能的影响

王玉华 佟士骅[△] 居海宁 张洁涵 徐迎辉

(上海中医药大学附属第七人民医院 心血管内科 上海 200137)

摘要 目的:探讨有氧康复运动对慢性心力衰竭(chronic cardiac failure, CHF)患者心室重构及血管内皮功能的影响。**方法:**78例CHF患者随机分为运动组(n=39)、对照组(n=39)。对照组给予常规内科药物治疗、日常活动能力训练,运动组在此基础上根据美国心脏病学会(American Heart Association, AHA)的《三阶段康复运动方案》进行有氧康复运动,共持续12周。比较两组治疗前后心脏结构和功能、血管内皮功能及生活质量的改善情况。**结果:**干预后,两组左室收缩末期内径(left ventricular end systolic diameter, LVESD)、左室舒张末期内径(left ventricular end-diastolic diameter, LVEDD)、明尼苏达心衰生活质量(Minnesota Living With Heart Failure, MLHF)评分、血清内皮素-1(Endothelin-1, ET-1)、血管紧张素 II(angiotensin II, Ang II)水平均明显减小,左室射血分数(left ventricular ejection fraction, LVEF)、6分钟步行试验(6 minute walking test, 6MWT)、血清一氧化氮(nitric oxide, NO)、降钙素基因相关肽(calcitonin gene-related peptide, CGRP)水平均明显升高,且运动组LVESD、LVEDD、MLHF评分、血清ET-1、Ang II水平明显低于对照组,LVEF、6MWT、血清NO、CGRP水平明显高于对照组,差异均有统计学意义($P<0.05$)。运动组干预期间心衰再入院率显著低于对照组,差异均有统计学意义($P<0.05$)。**结论:**有氧运动康复训练有助于改善CHF患者的血管内皮功能,延缓或逆转心室重构,提高生活质量,改善预后。

关键词:有氧康复运动;慢性心力衰竭;心室重构;血管内皮功能

中图分类号:R541.61 **文献标识码:**A **文章编号:**1673-6273(2018)11-2118-04

Influence of Aerobic Rehabilitation Exercise on the Ventricular Remodeling and Endothelial Function of Patients with Chronic Cardiac Failure

WANG Yu-hua, TONG Shi-hua[△], JU Hai-ning, ZHANG Jie-han, XU Ying-hui

(Department of Cardiology, Seventh People's Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, 200137, China)

ABSTRACT Objective: To explore the influence of aerobic rehabilitation exercise on the ventricular remodeling and endothelial function of patients with chronic cardiac failure (CHF). **Methods:** 78 cases of patients with CHF were randomly divided into the exercise group (n=39) and the control group (n=39). The control group was given routine drug treatment, ability training of daily living, while the exercise group was given aerobic rehabilitation exercise according to "three stages of rehabilitation exercise plan" by the American heart association (AHA) for 12 weeks based on the control group. The improvement of cardiac structure and function, endothelial function, and quality of life were compared between two groups before and after treatment. **Results:** After intervention, the levels of LVESD, LVEDD, serum ET-1, Ang II, and MLHF scores were reduced significantly in both groups, the levels of LVEF, 6MWT, NO, CGRP were significantly increased ($P<0.05$). The levels of LVESD, LVEDD, serum ET-1, Ang II, and MLHF scores in exercise group were significantly lower than those in the control group ($P<0.05$), the levels of LVEF, 6MWT, NO, CGRP in exercise group were significantly higher than those in the control group ($P<0.05$). The readmission rate because of heart failure in exercise group was significantly lower than that of the control group ($P<0.05$). **Conclusions:** Aerobic rehabilitation exercise is helpful to improve the vascular endothelial function, delay or reverse the ventricular remodeling and improve the quality of life and the prognosis for CHF patients.

Key words: Aerobic rehabilitation exercise; Chronic cardiac failure; Ventricular remodeling; Endothelial function

Chinese Library Classification(CLC): R541.61 **Document code:** A

Article ID: 1673-6273(2018)11-2118-04

慢性心力衰竭(CHF)是各种心脏病的终末阶段,患者心脏泵血功能障碍,常伴有心室重构、血管内皮功能损伤及肺淤血,无法满足机体组织的氧供,极易引起全身乏力,甚至是呼吸困

难。以往观点认为运动将进一步恶化心功能,故临床治疗时主张限制体力活动以减轻心脏负荷^[1-3]。近年来,越来越多的研究对上述观点提出质疑,尤其是随着有氧康复运动的快速发展,目前临床指南亦推荐联合有氧运动治疗^[4,5]。有研究表明有氧运动康复治疗可提高CHF患者的生活质量,降低住院率、病死率,现已逐渐成为CHF重要的非药物治疗方案^[6,7]。本研究在常规药物治疗的基础上联合有氧康复运动训练治疗CHF患者,旨在探讨其对患者心室重构及血管内皮功能的影响,现报道如下。

作者简介:王玉华(1969-),女,本科,副主任医师,研究方向:高血压及冠心病,电话:13816341777, E-mail: hua20201@163.com

[△] 通讯作者:佟士骅(1985-),男,本科,主治医师,研究方向:心脏康复, E-mail: tongshihua1985@126.com

(收稿日期:2017-10-05 接受日期:2017-10-27)

1 资料与方法

1.1 一般资料

收集 2014 年 1 月~2015 年 12 月我院心内科收治的 78 例 CHF 患者。入组标准: ① 符合《慢性心力衰竭诊断治疗指南(2007 年版)》中 CHF 诊断标准^[6],并经超声心电图、胸片或冠状动脉造影等影像学检查确诊; ② 美国纽约心脏病协会(NYHA)心功能 II-IV 级; ③ 排除严重心律失常、急性心肌梗死、肺栓塞、房室传导阻滞及严重肺肝肾功能障碍者。其中,男 42 例,女 36 例;年龄 48~79 岁,平均(61.1±6.4)岁;病程 3~7 年,平均(4.5±1.6)年;原发病:冠心病 42 例,高血压心脏病 18 例,扩张型心脏病 13 例,陈旧性心肌梗死 5 例。按照随机数字表法将 78 例 CHF 患者随机分为运动组、对照组,每组各 39 例。两组患者在性别构成比、年龄、病程、NYHA 分级及原发病等基本信息方面比较差异均无统计学意义($P>0.05$),具有可比性。本研究设计方案经医院伦理委员会审查通过,均获得患者或监护人知情同意。

1.2 治疗方法

所有患者入院后均按照《慢性心力衰竭诊断治疗指南(2007 年版)》^[6]给予规范的内科治疗,包括卧床休息、控制血压、吸氧、降糖调脂、利尿剂,以及血管紧张素转换酶抑制剂(ACEI)和 β 受体阻滞剂等扩血管药物,同时进行适当的日常活动,未给予其他特殊运动训练。运动组在对照组治疗的基础上,按照美国心脏病学会(AHA)制定的《三阶段康复运动方案》^[9],结合患者的 NYHA 分级给予有氧康复运动治疗,共分为热身期、锻炼期及恢复期三个阶段,(1)热身期:以低热量热身运动为主,包括肌肉拉伸、慢走等,持续 10~15 min;(2)锻炼期:待身体适应后,开始快走、慢跑、哑铃、功率自行车、八段锦、太极拳等,可分段进行,每次持续 5 min;(3)恢复期:慢走、肌肉拉伸等放松运动 5~10 min。每周训练 4 次以上,共持续 12 周。干预期间,实时监控运动过程患者心率变化,并根据患者的 NYHA 分级调整

运动内容、强度及持续时间,一旦出现不适立即停止运动。

1.3 观察指标

1.3.1 心功能指标测定 采用 HP5500 型彩色多普勒超声心动图仪(美国 Philips 公司),通过 Simpson 法测定左心室射血分数(LVEF)、左室收缩末期内径(LVESD)、左心室舒张末期内径(LVEDD)。干预 6 个月后再次进行超声心动图检查,比较上述指标的变化。

1.3.2 血管内皮功能 入院次日清晨采集空腹静脉血 10 mL, 3 000 r/min 离心 10 min 后去除上清液,留取血浆置于 EP 管中,保存于 -20℃ 冰箱备检。其中一氧化氮(NO)采用硝酸盐还原酶法测定,AngII 采用酶联免疫吸附法(ELISA)测定,内皮素 -1(ET-1)、降钙素基因相关肽(CGRP)采用放射免疫法测定。试剂盒购自武汉华美生物工程有限公司,所有操作均严格按使用试剂的说明书进行。

1.3.3 其他指标 分别于干预前后进行 6 分钟步行实验的距离(6MWT)、明尼苏达心力衰竭生活质量问卷(MLHF)评估患者的运动能力及生活质量改善情况,其中 MLHF 共涵盖 21 个条目,为 0~5 级共六级评分,分值范围为 0~105 分,得分越高说明生活质量越差;记录两组患者干预期间心衰再入院率。

1.4 统计学方法

采用 SPSS20.0 版统计软件包分析处理数据,计量资料以($\bar{x} \pm s$)表示,采用成组和配对 t 检验,计数资料以率表示,组间比较采用 χ^2 检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组干预前后心功能指标变化的比较

干预前,两组各心功能指标比较差异均无统计学意义($P>0.05$);干预后,两组 LVESD、LVEDD 均明显减小,LVEF 均明显升高,且运动组 LVESD、LVEDD 明显低于对照组,LVEF 明显高于对照组,差异均有统计学意义($P<0.05$)。见表 1。

表 1 两组干预前后心功能指标的比较($\bar{x} \pm s$)

Table 1 Comparison of the cardiac parameters before and after intervention between two groups($\bar{x} \pm s$)

Parameter	Exercise group(n=39)		Control group(n=39)	
	Before intervention	After intervention	Before intervention	After intervention
LVESD(mm)	40.59±3.57	35.81±1.46 [°]	40.06±3.81	37.24±2.39 [°]
LVEDD(mm)	61.06±6.63	54.96±4.60 [°]	62.53±6.09	58.24±5.43 [°]
LVEF(%)	55.62±6.26	69.53±5.47 [°]	54.14±5.59	63.16±5.91 [°]

Note: Compared with before intervention, [°] $P<0.05$; Compared within groups at the same phase, [°] $P<0.05$.

2.2 两组干预前后内皮功能指标的比较

干预前,两组各内皮功能指标比较差异均无统计学意义($P>0.05$);干预后,两组血清 NO、CGRP 水平均较干预前明显升高,血清 ET-1、Ang II 水平均较干预前明显降低,且运动组血清 NO、CGRP 水平均明显高于对照组,血清 ET-1、Ang II 水平均显著低于对照组,差异均有统计学意义($P<0.05$),见表 2。

2.3 两组干预前后 6MWT、MLHF 评分及心衰再入院率的比较

干预前,两组 6MWT、MLHF 评分比较差异均无统计学意义($P>0.05$)。干预后,两组 6MWT 均较干预前明显升高,MLHF 评分均较干预前明显降低,且运动组 6MWT 明显高于对照组,

MLHF 评分显著低于对照组,差异均有统计学意义($P<0.05$)。运动组干预期间心衰再入院率显著低于对照组,差异均有统计学意义($P<0.05$),见表 3。

3 讨论

CHF 是一种复杂的临床综合征,表现为心脏结构、功能异常,心室充盈及射血功能受损,其发病机制尚不十分清楚,可能涉及心肌与骨骼肌细胞的有氧代谢、能量转运、促炎症细胞因子、血管内皮功能紊乱及交感神经系统活动等诸多方面,其中交感神经系统和肾素-血管紧张素-醛固酮系统(RAAS)的激

表 2 两组干预前后内皮功能指标的比较($\bar{x} \pm s$)Table 2 Comparison of the endothelial function parameters before and after intervention between two groups($\bar{x} \pm s$)

Parameter	Exercise group(n=39)		Control group(n=39)	
	Before intervention	After intervention	Before intervention	Before intervention
NO($\mu\text{mol/L}$)	34.59 $\pm$ 6.57	92.81 $\pm$ 5.46 [°]	35.06 $\pm$ 6.81	77.24 $\pm$ 5.39
ET-1(ng/L)	23.06 $\pm$ 4.63	18.96 $\pm$ 4.60 [°]	24.13 $\pm$ 4.09	21.24 $\pm$ 5.43
CGRP (mg/L)	21.39 $\pm$ 6.16	57.73 $\pm$ 10.27 [°]	20.78 $\pm$ 5.19	42.36 $\pm$ 8.21
Ang II(ng/L)	103.59 $\pm$ 13.12	61.06 $\pm$ 9.10 [°]	107.83 $\pm$ 17.18	91.76 $\pm$ 11.29 [°]

Note: Compared with before intervention, [°] $P < 0.05$; Compared within groups at the same phase, [°] $P < 0.05$.

表 3 两组干预前后 6MWT、MLHF 评分及心衰再入院率的比较

Table 3 Comparison of the 6MWT, MLHF score and and readmission rate because of heart failure before and after intervention between two groups

Parameter	Exercise group(n=39)		Control group(n=39)	
	Before intervention	After intervention	Before intervention	Before intervention
6MWT(m)	314.65 $\pm$ 38.07	517.23 $\pm$ 57.40 [°]	306.12 $\pm$ 41.51	436.80 $\pm$ 55.23 [°]
MLHF score	34.13 $\pm$ 2.47	12.01 $\pm$ 1.51 [°]	35.06 $\pm$ 2.23	19.96 $\pm$ 1.12 [°]
Readmission rate because of heart failure	1(2.6)		6(15.4)	

Note: Compared with before intervention, [°] $P < 0.05$; Compared within groups at the same phase, [°] $P < 0.05$.

活是造成心脏功能不断恶化的主要原因^[10-12]。目前,该病仍采用药物为主的综合治疗,效果并不理想。随着心衰康复领域的发展,临床指南均推荐采用运动治疗,强调心脏康复在 CHF 综合治疗中的重要性和必要性。越来越多的研究显示有氧运动能够促进 CHF、冠心病、心绞痛等患者改善心脏功能,提高生活质量,但其机制尚不明确^[13-15]。

既往对 CHF 患者的康复运动多局限于住院期间,且以指导为主,缺乏系统性,强度和效果均不令人满意,尤其对出院后远期心脏功能及生活质量的影响仍未形成一致意见^[16,17]。Koufaki 等^[18]研究表明康复运动效果具有明显可逆性,中断 2 周后运动效果即开始下降,若中断 5 周,其效果将下降超过 50%。本研究对 CHF 患者进行为期 12 周连续、系统的有氧康复运动训练,超声心动图结果显示运动组 LVESD、LVEDD 明显减小,LVEF 明显升高,较对照组明显改善,与 Alves 等^[19]研究一致,表明有氧康复运动能够改善心脏的收缩、舒张功能,抑制甚至逆转左心室重构,改善心脏射血。

血管内皮功能障碍在 CHF 的发生、发展中发挥至关重要的作用,许多主要不良心脏事件(MACE)的发生均与内皮功能损伤密切相关^[20-22]。研究显示 CHF 患者多组织器官均存在不同程度的缺血、缺氧以及儿茶酚胺分泌增加等病理改变,诱发脂质过氧化,进而造成血管内皮结构或功能损伤,后者又可进一步加重 CHF 的病情的发生,形成恶性循环,而有氧运动有助于降低儿茶酚胺浓度、炎症反应、氧化应激及内皮功能障碍的标志物^[23,24]。改善、评估进而保护血管内皮功能对 CHF 的防治具有重要临床意义。本研究中,两组干预后 NO、CGRP 明显升高,ET-1、Ang II 明显降低,且运动组的改善幅度明显优于对照组,说明有氧运动能够减轻 CHF 患者的血管内皮功能损伤,改善神经内分泌系统,可作为 CHF 常规治疗的重要环节^[25]。此外,有氧康复运动对患者的运动耐力、生活质量也有明显改善

作用,有助于降低再住院率。

综上所述,CHF 患者在常规治疗的同时给予有氧运动康复训练有助于改善患者的血管内皮功能,延缓或逆转心室重构,提高患者生活质量,改善预后,是非药物治疗的一种有效手段。鉴于本研究样本量有限,观察时间尚短,长期有氧运动的效果仍后期继续积累样本进一步探讨。

参考文献(References)

- Gielen S. Exercise training in heart failure: which training modality works best?[J]. Journal of Applied Physiology, 2017, 123(2): 442-443
- Varma N, Sogaard P, Bax JJ, et al. Interaction of Left Ventricular Size and Sex on Outcome of Cardiac Resynchronization Therapy Among Patients With a Narrow QRS Duration in the EchoCRT Trial[J]. J Am Heart Assoc, 2018 May 27; 7(11)
- Senni M, Paulus WJ, Gavazzi A, et al. New strategies for heart failure with preserved ejection fraction: the importance of targeted therapies for heart failure phenotypes[J]. European Heart Journal, 2014, 35(40): 2797-2815
- Greaves CJ, Wingham J, Deighan C, et al. Optimising self-care support for people with heart failure and their caregivers: development of the Rehabilitation Enablement in Chronic Heart Failure (REACH-HF) intervention using intervention mapping [J]. Pilot and Feasibility Studies, 2016, 2(23): 37-54
- Sindler AL, Reyes R, Chen B, et al. Age and exercise training alter signaling through reactive oxygen species in the endothelium of skeletal muscle arterioles[J]. J Appl Physiol, 2013, 114(5): 681-693
- 薛礼, 茶春喜, 罗仁, 等. 运动疗法对慢性心力衰竭患者预后的影响[J]. 中华实用诊断与治疗杂志, 2013, 27(3): 231-233
- Xue Li, Cha Chun-xi, Luo Ren, et al. Effect of exercise therapy on the prognosis of patients with chronic heart failure [J]. Journal of Chinese Practical Diagnosis and Therapy, 2013, 27(3): 231-233
- Tully P J, Selkow T, Bengel J, et al. A dynamic view of comorbid

- depression and generalized anxiety disorder symptom change in chronic heart failure: the discrete effects of cognitive behavioral therapy, exercise, and psychotropic medication [J]. Disability and rehabilitation, 2015, 37(7): 585-592
- [8] 中华医学会心血管病学分会, 中华心血管病杂志编辑委员会. 慢性心力衰竭诊断治疗指南 [J]. 中华心血管病杂志, 2007, 35(12): 1076-1095
- Chinese Society of Cardiology of Chinese Medical Association Editorial Board of Chinese Journal of Cardiology. Guidelines for the diagnosis and management of chronic heart failure[J]. Chinese journal of cardiology, 2007, 35(12): 1076-1095
- [9] Guazzi M, Adams V, Conraads V, et al. American Heart Association. EACPR/AHA Scientific Statement. Clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations[J]. Circulation, 2012, 126(18): 2261-2274
- [10] Kitzman D W, Brubaker P H, Herrington D M, et al. Effect of endurance exercise training on endothelial function and arterial stiffness in older patients with heart failure and preserved ejection fraction: a randomized, controlled, single-blind trial[J]. Journal of the American College of Cardiology, 2013, 62(7): 584-592
- [11] Hirai DM, Musch TI, Poole DC. Exercise training in chronic heart failure: improving skeletal muscle O₂ transport and utilization [J]. Am J Physiol Heart Circ Physiol, 2015, 309(9): H1419-439
- [12] Zucker IH, Schultz HD, Patel KP, Wang H. Modulation of angiotensin II signaling following exercise training in heart failure[J]. American Journal of Physiology - Heart and Circulatory Physiology, 2015, 308(8): 781-791
- [13] GROEHS RV, Toschi-Dias E, Antunes-Correa LM, et al. Exercise training prevents the deterioration in the arterial baroreflex control of sympathetic nerve activity in chronic heart failure patients [J]. Am J Physiol Heart Circ Physiol, 2015, 308(9): H1096-1102
- [14] Sandri M, Viehmann M, Adams V, et al. Chronic heart failure and aging - effects of exercise training on endothelial function and mechanisms of endothelial regeneration: Results from the Leipzig Exercise In European Journal of Preventive Cardiology, 2016, 23(4): 1120-1133
- [15] Ades PA, Keteyian SJ, Balady GJ, et al. Cardiac Rehabilitation Exercise and Self Care for Chronic Heart Failure [J]. JACC Heart failure, 2013, 1(6): 540-547
- [16] Haack KKV, Zucker IH. Central Mechanisms for Exercise Training-Induced Reduction in Sympatho-Excitation in Chronic Heart Failure [J]. Autonomic neuroscience: basic & clinical, 2015, 10(2): 44-50
- [17] Pandey A, Parashar A, Kumbhani D, et al. Exercise Training in Patients with Heart Failure and Preserved Ejection Fraction: A Meta-analysis of Randomized Control Trials [J]. Circulation Heart Failure, 2017, 10(8): 47-59
- [18] Koufaki P, Mercer T H, George K P, et al. Low-volume high-intensity interval training vs continuous aerobic cycling in patients with chronic heart failure: a pragmatic randomised clinical trial of feasibility and effectiveness [J]. Journal of rehabilitation medicine, 2014, 46(4): 348-356
- [19] ALVES JP, NUNES RB, STEFANI GP, et al. Resistance training improves hemodynamic function, collagen deposition and inflammatory profiles: experimental model of heart failure [J]. PLoS One, 2014, 9(10): e110317
- [20] Park KH, Park WJ. Endothelial dysfunction: clinical implications in cardiovascular disease and therapeutic approaches [J]. Journal of Korean medical science, 2015, 30(9): 1213-1225
- [21] Sharma K, Kass DA. Heart failure with preserved ejection fraction: mechanisms, clinical features, and therapies [J]. Circ Res, 2014, 115(1): 79-96
- [22] Haykowsky MJ, Brubaker PH, Morgan TM, et al. Impaired aerobic capacity and physical functional performance in older heart failure patients with preserved ejection fraction [J]. J Gerontol A Biol Sci Med Sci, 2013, 68(8): 968-975
- [23] Beavers KM, Miller ME, Rejeski WJ, et al. Fat mass loss predicts gain in physical function with intentional weight loss in older adults [J]. J Gerontol A Biol Sci Med Sci, 2014, 69(10): 1306-1311
- [24] Sandri M, Viehmann M, Adams V, et al. Chronic heart failure and aging-effects of exercise training on endothelial function and mechanisms of endothelial regeneration: Results from the Leipzig Exercise Intervention in Chronic heart failure and Aging (LEICA) study [J]. European Journal of preventive cardiology, 2016, 23(4): 349-358
- [25] Kitzman DW, Brubaker PH, Herrington DM, et al. Effect of endurance exercise training on endothelial function and arterial stiffness in older patients with heart failure and preserved ejection fraction[J]. J Am Coll Cardiol, 2013, 62(7): 584-592
- (上接第 2097 页)
- [23] Hospodar P, Guzman, Johnson P, et al. Treatment of displaced calcaneus fractures using a minimally invasive sinus tarsi approach[J]. Orthopedics, 2013, 31(9): 11-12
- [24] Whittaker JL, Stokes M. Ultrasound Imaging and Muscle Function [J]. J Orthop Sports Phys Ther, 2011, Jun 7[Epub ahead of print]
- [25] Weber MA, Wormsbecher S, Krix M, et al. Contrast-enhanced ultrasound of skeletal muscle [J]. Radiology, 2011, 51(6): 497-505
- [26] Endo Y. The role of ultrasonography in the diagnosis of gluteal muscle contracture[J]. Ultrasound Q, 2011, 27(2): 115
- [27] Roch-Bras F, Daurès JP, Legouffe MC, et al. Treatment of chronic knee synovitis with arthroscopic synovectomy: longterm results [J]. J Rheumatol, 2002, 29(6): 1171-1175
- [28] 李晓捷. 实用小儿脑性瘫痪康复治疗技术[M]. 北京: 人民卫生出版社, 2009, 12-12
- Li Xiao-jie. A practical technique for the rehabilitation of cerebral palsy in children[M]. Beijing: People's Health Press, 2009, 12-12
- [29] Mao HF, Chen WY, Yao G, et al. Cross-cultural adaptation and validation Of the Quebec User Evaluation of Satisfaction with Assistive Technology: the development of the Taiwanese version[J]. Clin Rehabil, 2010, 24(5): 412-421
- [30] Nakamura H, Nagashima M, Ishigami S, et al. The anti-rheumatic effect of multiple synovectomy in patients with refractory rheumatoid arthritis[J]. Int Orthop, 2000, 24(5): 242-245