

Training on Cardiopulmonary Fitness

Subjects: **Rehabilitation**

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Heart failure (HF) is a common disease with an increasing prevalence worldwide and it is characterized by a low five-year survival of 35–55%, which affects cardiac function, exercise tolerance, and the daily life of patients. Cardiac rehabilitation is defined as a set of activities that aims to provide patients with heart disease with the best physical, mental, and social conditions, therefore, reducing the risk of death and acute events related to their illness. Previous studies have demonstrated that cardiac rehabilitation with physical exercise was beneficial to physical fitness, cardiac function, and quality of life in HF patients.

interval training

continuous training

heart failure

meta-analysis

1. Introduction

Heart failure (HF) is a common disease with an increasing prevalence worldwide and it is characterized by a low five-year survival of 35–55% ^[1], which affects cardiac function, exercise tolerance, and the daily life of patients ^{[2][3]}. Previous studies have demonstrated that cardiac rehabilitation with physical exercise was beneficial to physical fitness, cardiac function, and quality of life in HF patients ^{[4][5]}. At present, various exercise programs are widely applied to cardiac rehabilitation, in which continuous training (CT) and interval training (IT) are the main forms of exercise ^{[6][7]}. However, there continues to be disagreement on whether or not IT and CT can significantly improve the cardiac function and functional capacity of patients with cardiovascular disease; the effectiveness between the two exercise programs is similar and it cannot be distinguished which exercise program is better ^{[8][9]}.

VO₂peak has been considered to be the best predictor of survival in cardiovascular diseases and it has been used in many previous studies to measure patients' cardiorespiratory fitness ^{[10][8][9][11][12]}. The VE/VCO₂ slope is inversely related to cardiac output at peak exercise and is at least partly explained by a decrease in pulmonary perfusion ^[13]. Bruna (2019) suggested that high intensity interval training was more effective than moderate continuous interval training for improving VO₂peak, while the effect was not significant for improving left ventricular ejection fraction (LVEF) between the two exercise programs ^[14]. Mansueto (2018) suggested that high intensity interval training was superior to moderate continuous interval training for improving VO₂peak in HF patients with reduced ejection fraction but the superiority disappeared when they performed a subanalysis ^[15].

2. Development and Findings

This systematic literature review with meta-analysis suggests that IT elicits greater improvements in VO₂peak, LVEF, and 6MWD than CT, which is similar to previous meta-analyses comparing IT with CT in HF ^{[14][16]} and

coronary heart disease patients [17][18]. The strengths of this study as compared with previous studies is that more studies were retrieved to compare the effects on cardiorespiratory fitness and exercise tolerance in HF patients between IT and CT. In addition, several indispensable outcomes for HF patients were adopted to measure the effects between the two exercise programs, and therefore provided enough basis for cardiac rehabilitation.

The VO₂peak is considered to be the best predictor of survival in cardiovascular diseases [19][20]. Previous studies have indicated that a peak aerobic power ≤ 10 mL/kg/min is a strong predictor of a poor prognosis in patients with HF [21][22]. The meta-analysis showed that IT significantly improved VO₂peak of 2.08 mL/kg/min in patients with HF than CT. In addition, the results of the subgroup analyses suggested that IT as compared with CT was more significant for improving patients' VO₂peak with "intervention duration <12 weeks" than "intervention duration ≥ 12 weeks". Meanwhile, the intensity of 60–80% HRpeak can gain better exercise effects than the intensity of 80–100% HRpeak for HF patients. The reason why a lower intensity gained a better effect may be that maximal intensity of IT has a deeper impact on patients' hearts than a relatively lower intensity, which may not be beneficial to recovery. Previous clinical studies have shown that every 1 mL/kg/min increment in VO₂peak leads to the mortality of male and female patients with cardiovascular diseases reducing by 16% and 14%, respectively [12]. The mechanism of IT improving VO₂peak may be reflected in the following aspects: (1) the intensity of IT is relatively higher than CT, which may result in an increase in plasma volume and erythrocyte volume [23][24]. (2) IT improves venous drainage and increases stroke output as well as decreases the resistance of blood flow [25]. (3) IT can increase activation of peroxisome proliferator-activated receptor- γ coactivator (PGC-1 α), which accelerates the mitochondrial biosynthesis process, which is essential to enhance the metabolism ability of skeletal muscle. Mitochondrial function is associated with aerobic physical fitness and plays an important pathophysiological role in cardiac patients [17][26]. Some previous studies have explored the potential physiological mechanism of IT for improving patients' cardiorespiratory fitness, but there was still no clear explanation. It may be influenced by intervention duration, exercise intensity, and individual physical capacity. Therefore, the physiological mechanism of IT for improving cardiorespiratory fitness needs further exploration.

The LVEF is a sensitive index that reflects the function of the left ventricular pump. It is more sensitive and reliable than stroke volume and cardiac index. It directly reflects the left ventricular ejection efficiency and indirectly reflects myocardial contractility [27]. The meta-analysis suggested that there was a significant difference in the LVEF between IT and CT (MD = 1.32, 95% CI 0.60 to 2.03, $p = 0.0003$). The mechanisms responsible for an increment in LVEF may be the following: (1) A higher exercise heart rate during IT increases the magnitude of the post-exercise alteration in left ventricular diastolic filling [28]. (2) Potential mechanisms responsible for altered left ventricular relaxation, in addition to prolonged elevated heart rate, include downregulation of cardiac β -adrenoceptors mediated by elevated catecholamines during exercise. In fact, circulating catecholamines are responsible for maintaining tachycardia during exercise [29]. (3) Exercise training leads to a partial correction of peripheral endothelial dysfunction in patients with HF [30].

The 6MWD is an indicator of the ability to perform daily life activities, which measures exercise tolerance. Improvement in the 6MWD has also been equated with improved quality of life in patients [31]. The meta-analysis suggested that IT significantly increased 6MWD more than CT in HF patients (MD = 25.67, 95% CI 12.87 to

38.47, $p < 0.0001$). The mechanism of IT responsible for increased 6MWD is that a high-intensity IT effort culminating near VO_{2max} , requires that mitochondrial oxidative phosphorylation is fueled by carbohydrate substrates and operates at or near maximal capacity for several consecutive minutes. This type of effort might also represent a greater metabolic challenge for the mitochondria than CT, during which anaerobic metabolism (glycolysis and phosphocreatine) contributes significantly to ATP production [32]. Finally, the acute effects on mitochondrial respiratory function of a relatively high-intensity IT that ultimately yields VO_{2max} and elicits improvements in muscle aerobic capacity [26].

The RER is the ratio of carbon dioxide emission to oxygen uptake. A value of RER equal to at least 1.0 is commonly used to describe adequate effort and motivation in HF patients [33]. The result suggested that there was no significance in RER between IT and CT (MD = 0.00, 95% CI -0.02 to 0.03, $p = 0.81$). The VE/VCO_2 slope is an important indicator reflecting exercise tolerance, and it is also an important predictor of death in patients with HF [34]. Risk of mortality is thought to increase when the value of the VE/VCO_2 slope is greater than 34 [35]. The non-significance of our result (SMD = 0.04, 95% CI -0.23 to 0.31, $p = 0.75$) between IT and CT is in agreement with previous studies [17][18]. HRrest is a useful clinical marker for cardiovascular disease assessment. Previous studies have shown that for every 10 beats per minute (bpm) increment in HRrest, there is a 14% increased risk for a clinical cardiovascular disease event [36]. The meta-analysis result showed that there was no significance in HRrest between the two exercise programs (MD = 0.15, 95% CI -3.00 to 3.29, $p = 0.93$). These outcomes still need to be further elucidated in large and well-designed studies.

There are some limitations to the meta-analysis as follows: (1) There are no previous studies that have explored the impact of different intensities of IT on HF patients, which makes the division of intensity difficult. In addition, in all the included studies, all patients were in the New York Heart Association (NYHA) functional class I–III, but there was no literature to provide detailed class information. In the future, different intensities of IT could be classified to investigate which one is the optimal intensity for HF patients with different NYHA classes. (2) There is significant heterogeneity with respect to the outcome of VO_{2peak} . Although various subgroups (i.e., exercise duration, exercise intensity of IT, and isocaloric consumption) were performed to explore heterogeneity, unwanted heterogeneity was still obvious, and the relatively small number of studies included in each subgroup could not effectively account for the heterogeneity underlying the various studies. (3) This meta-analysis is not registered and some outcomes are based on small sample sizes, which may affect the stability of the results. In addition, our results may be affected by publication bias. It is hoped that, in the future, more well-designed studies would further expand the meta-analysis results.

3. Conclusions

The evidence shows that interval training is better than continuous training for improving cardiorespiratory fitness and exercise tolerance of patients with heart failure. Moreover, the intensity of 60–80% peak heart rate of interval

training is the optimal choice for patients. It is hoped that, in the future, more well-designed studies would further expand the meta-analysis results.

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