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♦ Revisão Integrativa

AEROBIC EXERCISE TRAINING IN ACUTE HEART FAILURE PATIENTS:

AN INTEGRATIVE REVIEW.

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ABSTRACT

Introduction: Decompensated Heart Failure patients are characterized by functional dependence and low exercise tolerance. Aerobic exercise can improve symptoms, promoting functional capacity and an increase of exercise tolerance. However, the benefits of early rehabilitation for inpatients have not been validated yet. **Objective:** To identify the use of aerobic exercise training in acute heart failure patients and, as secondary objective, to determine the feasibility, safety and effectiveness of such intervention**. Methods:** An integrative review with a search in PubMed, Cumulative Index to Nursing and Allied Health Literature, Scientific Electronic Library Online and Cochrane Library was conducted on January of 2020, to identify randomized controlled trials comparing patients who performed aerobic exercise training during inhospital stay, with patients who only performed usual care, published from January 2014 to December 2019. Additional hand search was performed in the national repository of academic works. The search retrieved 381 articles. Only one met the inclusion criteria. **Results:** One RCT was identified, with an assessment of high risk of bias, comparing patients who performed in-bed cycloergometer with patients who performed the same intervention with non-invasive ventilation and control group. The use of non-invasive ventilation lead patients to present a better performance, but even patients without non-invasive ventilation had significantly better results than the ones who only performed the usual care. **Conclusions:** Despite the results pointing some benefits, there is insufficient data to determine the feasibility, safety and effectiveness of aerobic exercise training in acute heart failure inpatients. More research is needed to validate its use.

INTRODUCTION

Heart failure (HF) can be defined as an abnormality of the heart function or structure leading to reduced oxygen delivery throughout the body(Ponikowski et al., 2016). It is a growing global health challenge, with a great economic burden for the health system. The prevalence is approximately 1 to 2% of the population in developed countries, and this percentage rises above 10% in people over 70 years old(Cattadori, Segurini, Picozzi, Padeletti, & Anzà, 2018; Murphy, Ibrahim, & Januzzi, 2020). Due to its complex and progressive nature it usually results in adverse events, such as high rate of hospital readmission and mortality(Gary, Cress, Higgins, Smith, & Dunbar, 2012; Giallauria, Piccioli, Vitale, & Sarullo, 2018).

The major symptoms are exercise intolerance, dyspnea and fatigue. Decreased exercise tolerance is a hallmark feature in HF patients and may have many contributing factors, such as decreased cardiac output, peripheral muscle wasting, and autonomic imbalance(Dunlay, Griffin, Redfield, & Roger, 2017). It is an important health care problem associated with high morbidity, mortality and with reduced quality of life(Palmer, Bowles, Paton, Jepson, & Lane, 2018; Ponikowski et al., 2016; Tucker et al., 2019).

HF is a progressive disease, demonstrated by the patient's physical impairment. Exercise intolerance pushes the patient towards sedentary behaviors and consequently these behaviors lead to an even greater decline in functional capacity, with loss of aerobic capacity, muscle mass and muscle strength(Fukuta, Goto, Wakami, Kamiya, & Ohte, 2019; Lee, Chen, & Chien, 2017).

During the course of the disease patients often experience decompensation of their illness that lead them to a period of inhospital stay for properly compensation. During this period patients are frailer and also inactive, which conducts them to higher levels of functional dependence(Dunlay, Griffin, et al., 2017; Dunlay, Roger, & Redfield, 2017; Reeves et al., 2017; Reeves et al., 2016). It is very important to promote physical activity during the inhospital stay, integrating patients into cardiac rehabilitation (CR) phase one programs(Hansen et al., 2018; Piepoli et al., 2011; Ponikowski et al., 2016).

CR can be defined as a sum of activities that favorably influence the underlying causes of cardiovascular disease, so that the patients can obtain the best physical, psychological and social conditions, reassuming their role in society as normally as possible (Ana Abreu, Bettencourt, & Fontes, 2010; Bjarnason-Wehrens et al., 2010; Palmer et al., 2018; Piepoli et al., 2011).

The CR program is divided in three different phases, namely phase 1, which takes place during the inhospital stay period; phase 2, called the ambulatory phase and finally phase 3, called maintenance phase. In phase 1, patients are taught about their disease, the cardiovascular risk factors, the impact of the disease on their lives, the management and maintenance behavior that should be followed and finally patients begin to perform some physical activity in order to promote their functional capacity, to optimize the treatments and analyze the physiological heart response to activity itself. This is probably the most critical phase and more complex, since the patients are still decompensated and frail. Phase 2 takes place at an ambulatory gym inside the hospital, where patients can exercise according to a prescription after fulfilling a cardiopulmonary exercise testing and always under supervision of a specialized cardiac rehabilitation team. In phase 3 it is expected that patients continue to manage their therapeutic regimen adequately and accordingly to what they have learned on the previous phases. The continuum of the three phases guarantee a reduction of the cardiovascular risk and an improvement on the quality of life of these patients (A. Abreu et al., 2018; Bocalini, dos Santos, & Serra, 2008; Fukuta et al., 2019; Slimani et al., 2018).

Clearly it is important to clarify some concepts. Physical activity can be defined as any body movement produced by the voluntary contraction of the skeletal muscle, which causes energy expenditure above the basal level. It is often related to the development of the activities of daily living. Exercise is known as a sub-category of the physical activity in which planned, structured and repetitive body movements are performed, in order to maintain or increase one or more physical attributes, in a given period of time (ACSM, 2018).

The core component of CR is the exercise training(ACSM, 2018); within consensus, European guidelines have incorporated a class IA recommendation for regular aerobic exercise in HF patients. This non-pharmacological treatment has several benefits and improves functional capacity, symptoms relief and health-related quality of life. It also reduces mortality and rates of hospital readmission for decompensated HF(ACSM, 2018; Ponikowski et al., 2016; Seo et al., 2019) .

The exercise prescription is designed for a specific purpose and it is usually developed by rehabilitation specialists based on the patient's condition, motivation and goals. This program can be carried out in an inpatient or outpatient phase and should be planned according to the FITT-VP parameters (Frequency, Intensity, Time, Type, Volume and Progression)(ACSM, 2018; Seo et al., 2019). The objective of this model is to assist professionals in the development of an individualized training plan optimized for the patient's clinical condition and

comorbidities, with the aim of improving physical fitness and health(Hansen et al., 2018; Seo et al., 2019).

According to the previous, an integrative review was conducted with the primary objective to identify the use of aerobic exercise training in acute heart failure patients and, as secondary objective, to determine the feasibility, safety and effectiveness of such intervention, knowing that inhospital stay is the critical period to early begin to perform cardiac rehabilitation.

Our working research question is: Is there evidence about the use of aerobic exercise training in acute heart failure patients, and if so, is it feasible, safe and effective?

METHODS

An integrative review of the literature was the research method of choice since no reviews were identified on this topic. Exercise training is a new/emerging topic in acute heart failure patients that would benefit of a more comprehensive approach(RJ, 2016Dec). The starting point for this research were the primary and secondary objectives that outlined the research strategy. There for, the PICO strategy was used to ensure that all significant components of the research question were attended. Thus, the review question following the PICO strategy was: (P) heart failure inpatients, (I) aerobic exercise training, (C) patients who performed the standard care and (O) feasibility, efficacy and safety of exercise. For outcome assessment it was considered that efficacy is related to an improvement of patient's functional capacity during the length of stay and the safety is related to the absence of adverse events during the performance of exercises. If exercise is efficient and safe, then it is also feasible to be implemented during the stabilization phase of the disease.

It was decided to only include randomize controlled trials (RCT) where rehabilitation interventions, namely aerobic exercise training was performed to improve patient's functional capacity during the inhospital stay. The full inclusion criteria are presented in Table 1.

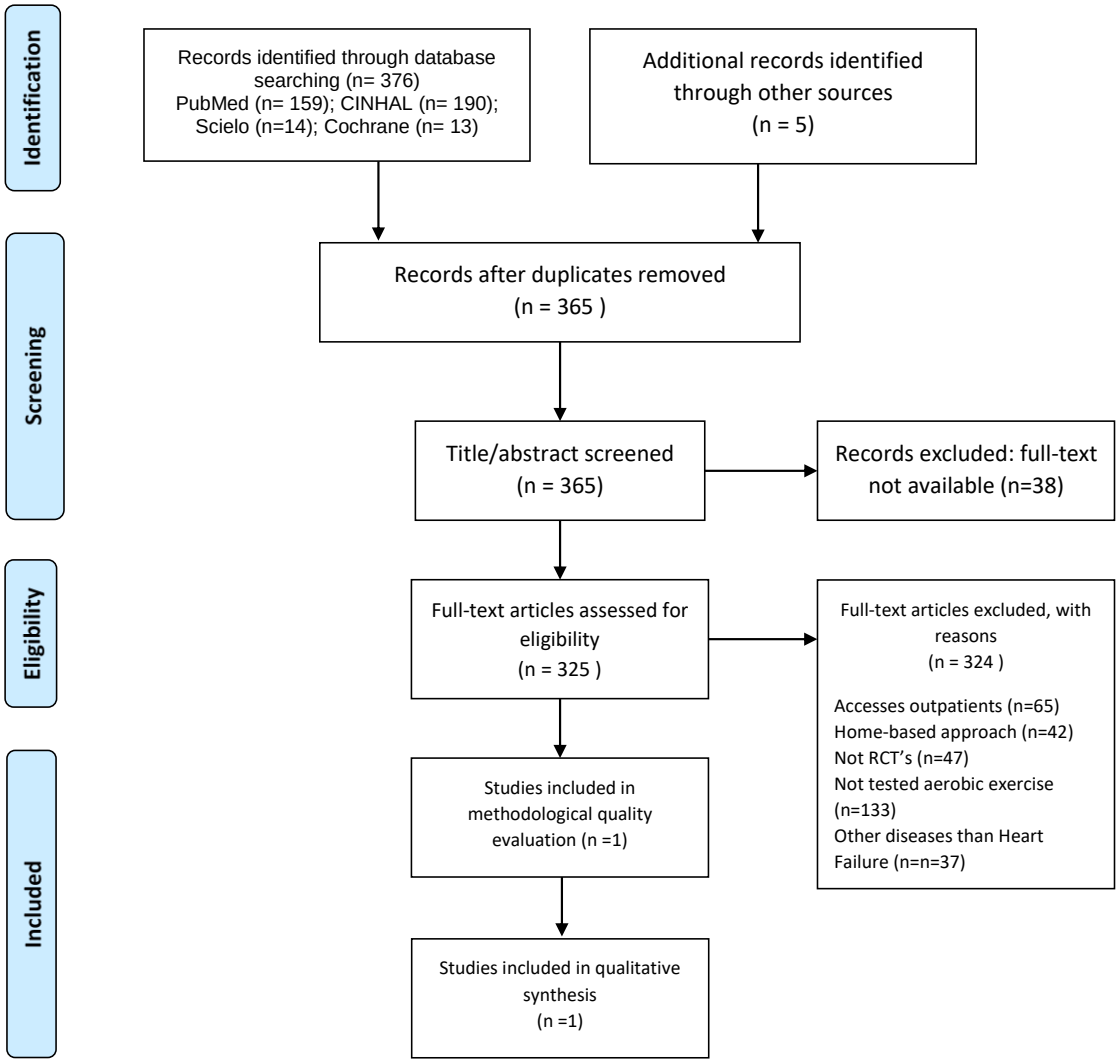
Table 1 – inclusion criteria for selected studies

Inclusion criteria
Hospitalized patients with decompensated heart failure
Adults only
Randomized comparison
Intervention was exercise training (whether aerobic, strength or respiratory or a mixture of different modalities)
Outcomes must be functional capacity (evaluated by any functional capacity tool, especially the six-minute walking test [6MWT]) and safety of the intervention
Control group should not perform exercise training
Studies published after January 2014 and before 2020, in english.

Two reviewers (BMD and IJO) independently search four databases: 1) PubMed, 2) Cumulative Index to Nursing and Allied Health Literature (CINHAL), 3) Scientific Electronic Library Online (SciELO) and 4) Cochrane Library; the research was performed on January of 2020. Additional hand search was performed in the national repository of academic works in order to identify relevant unpublished studies. The Medical Subject Headings (MeSH) were used to select the more suitable terms to respond to the objectives of this review. The descriptors, in conjunction with *Boolean* operators, were the following: ("Heart failure" OR "Cardiac Failure" OR "Congestive Heart Failure" OR "Heart Decompensation" OR "Myocardial Failure") AND ("Exercise" OR "Acute Exercise" OR "Aerobic Exercise" OR "Exercise Training") AND ("Cardiac rehabilitation" OR "rehabilitation"). In three of the databases different search limitations were applied to retrieve the articles. For PubMed, search limits for only RCT were applied, limiting the search for papers in English and with adults +19 years; at CINAHL the search was limited to the English language and at the Cochrane Library after the search phrase the results were limited by health topic, heart and circulation, and afterwards the search was limited for a specific clinical condition, heart failure.

This search returned 381 articles that were then screened by two independent reviewers (BMD and IJO) by title and abstract for eligibility. Most articles were excluded since they studied outpatients or did not test aerobic exercise. Full detailed retrieval and selection of articles was performed according to PRISMA statement(Moher et al., 2015) and is shown in figure 1.

Figure 1 - PRISMA flow diagram



For risk of bias assessment, a revised Cochrane risk of bias tool for randomized trials(Sterne et al., 2019) was used comprising five domains: randomization process, effect of assignment to intervention, missing outcome data, measurement of the outcome and selection of the reported result. The possible outcome of the assessment is "high risk of bias", "some concerns" or "low risk of bias". Two reviewers independently assessed the sole study included for methodological assessment (BMD and IJO) and consensus was reached in all domains. The assessment, by domains was as followed: randomization process – high risk of bias; effect of assignment to intervention – high risk of bias; missing outcome data – low risk of bias;

measurement of the outcome – some concerns; and selection of the reported result – some concerns. The overall risk of bias assessment is of high risk.

For data extraction a matrix was previously prepared which was independently used by the reviewers, comprising the following items: authors, study type, sample, intervention and results.

RESULTS

A total of 381 documents were retrieved, 376 on databases and five on the national repository of academic works. After duplicate removal, 365 articles were screened first by title and abstract and afterwards by full-text allowing to identify one article(Oliveira et al., 2018).

An overview of the article with the summary of the main characteristics can be found in table 2.

Table 2 - Summary of study's main characteristics

Authors	Study	Sample	Intervention	Results
Oliveira et al., 2017	Prospective multiple-armed randomized controlled study	29 in patients with acute heart failure and previous Doppler echocardiography with left ventricle ejection fraction < 30%	Control: standard medical treatment; Group ET+Sham: exercise training and placebo, once a day for eight days; Group ET+NIV: exercise training and non-invasive ventilation, once a day for eight days. At day one all patients were submitted to clinical evaluation: spirometry, blood sample (brain natriuretic peptide and high sensitivity C-reactive protein, six-minute walk test and maximal inspiratory pressure. Evaluation was repeated at day 10. After protocol all patients continued receiving only medical treatment and were followed until discharge or transfer to intensive care unit. Exercise protocol: aerobic exercise on an unloaded in-	None of the patients in either exercise groups had adverse events or required exercise interruption. The six-minute walk test distance was greater in ET+NIV (Δ120±72 m) than ET+Sham (Δ73±26m) and control (Δ45±32m; p<0,05). Total exercise time was greater (128±10 vs. 92±8 min; p<0,05) and dyspnea was lower (3±1 vs. 4±1; p<0,05) in ET+NIV than ET+Sham. The ET+NIV group had shorter hospital stay

			bed cycle ergometer for 20 minutes or less, until limit of tolerance; heart rate continuous monitoring during exercise; systolic and diastolic arterial pressures were obtained by auscultatory method; blood lactate was collected during exercise every two minutes, at rest and at the end of exercise and; "shortness of breath" assessment at exercise cessation by Borg's category ratio scale. Non-invasive ventilation: Bi-level ventilator applied via oronasal mask in two conditions a) bi-level positive airway pressure ventilation (inspiratory positive airway pressure 14 cmH_2O and expiratory positive airway pressure 8 cm H_2O without supplementary oxygen) and; b) sham ventilation (inspiratory positive airway pressure 4 cmH_2O and expiratory positive airway pressure 4 cm H_2O without supplementary oxygen).	(17±10 days) than ET+Sham (23±8 days) and control (39±15 days) groups (p<0,05). Total exercise time in ET+Sham and ET+NIV had significant correlation with length of stay (r=-0,75; p=0,01).

DISCUSSION

A total of 381 articles were retrieved and only one met the inclusion criteria. The authors used three homogeneous groups of patients: two interventions groups and one control group, hypothesizing that aerobic exercise training (AET) performed with non-invasive ventilation (NIV) is effective in acute HF patients. The third group, AET alone, was used to assess the safety of the intervention in acute HF patients. Thereby, the use of three groups allowed to test not only the use of NIV with AET but also the safety and effectiveness of AET alone using the six-minute walk test, which has been previously used in studies with HF patients(Giannitsi et al., 2019; Lakdizaji , Hassankhani, **Mohajjel aghda**m , & Khalilzad 2015). However, some aspects of the intervention must be addressed; it should be emphasized that the exercise training intervention comprised a very restricted typology of exercise – only cycloergometer,

which is very limited in order to truly infer about aerobic exercise tolerance and feasibility. Patients only exercise in bed and the workload is not known. Also, information about heart rate variation would be important, in order to infer about exercise intensity(ACSM, 2018; Cattadori et al., 2018).

The results suggest that aerobic exercise performed during the phase of stabilization is safe, since there were no adverse events in either intervention groups. It must be highlighted that the sample of patients presented very low function capacity level and are of high risk of decompensation – NYHA class IV patients are the ones with resting symptoms of dyspnea and exertion(Martens, Jacobs, Dupont, & Mullens, 2018) and left ventricular ejection fraction <30% that represents a significant impairment of ventricular filing which may unable the ability of patients to perform exercise(Fukuta et al., 2019; Jorge Alves et al., 2010; O'Connor et al., 2009). These patients are often excluded from trials involving exercise(Morris & Chen, 2019) and their enrollment in such a complex intervention is of great value and probably justifies the limited typology of exercise used, since safety and feasibility has never been tested before in acute HF inpatients.

This specific issue – exercise and decompensated patients is very delicate, since patients are unstable and safety concerns must be at the top of the list of priorities; maybe that is the main reasons why there is a lack of evidence in the field(Morris & Chen, 2019) and may explain one of the study's limitation: a small sample size. Meanwhile, guidelines often recommend that earlier physical activity should be engaged as soon as patients are able to(ACSM, 2018; Piepoli et al., 2011; Ponikowski et al., 2016); however, these same guidelines give imprecise orientations about the amount of exercise that patients must perform. It is recommended to walk short-to-moderate distances, with minimal or no assistance, three to four times a day, progressing to independent ambulation; upper body movement exercises and minimal stair climbing. For the previous it is noticeable that these recommendations are unclear about the time and duration of exercise(ACSM, 2016) and most important, there is no information about the effectiveness of the intervention.

Regarding safety, which is of major concern and it is also emphasized in the article selected, guidelines refer to the limits that must not be exceeded and elucidate about the signs and symptoms that should be of concern; namely the level of exertion, heart rate variation and electrocardiographic rhythm changes(ACSM, 2018; Alvarez, Hannawi, & Guha, 2016; Cattadori et al., 2018).

Reeves *et al* (2017), published a pilot study where they describe an intervention of earlier cardiac rehabilitation for heart failure inpatients such as the authors of the selected article did. This intervention started during hospitalization period and continue for a period of 12 months where functional capacity was accessed in order to test the effectiveness of exercise training; however, in this study no evaluation at discharge was performed and no exercise training protocol or intervention was described(Reeves et al., 2017), which is in contrast to the study selected for this revision. Authors address as limitations the fact that this is pilot study with a small sample size and not designed or powered to assess efficacy or safety of the intervention. Only the feasibility was safeguarded and tested.

As it can be clearly observed, in the study selected(Oliveira et al., 2018) and on this last study referred(Reeves et al., 2017) there is always the same limitations: the inability to firmly confirm the feasibility, safety and effectiveness of exercise training during the phase of stabilization. This limitations, together with the recommendations of guidelines creates a window of opportunities for investigators to develop interesting studies to test AET for decompensated HF patients.

The results of the included study for review must be carefully interpreted since the risk of bias assessment showed that this study has a high risk of bias. Despite that, these results encourage the development of further research on the viability, safety and efficacy of AET for inpatients with heart failure.

In the future, RCT with a significant sample size must be performed, following the steps that other investigators did, following the recommendations and safety concerns and aiming to innovate and test a structured AET protocol.

CONCLUSION

The present integrative review of literature presents some limitations: some studies may have been disregarded by limiting the search to four databases and English language publication, the high risk of bias of the included study and, as main limitation, the fact that only one study met the inclusion criteria. For this reason, there is very limited evidence to discuss the theme and reach some further conclusions. In addition to the fact that there is only one study that meets the criteria, it corresponds to a pilot study and as such, it presents little robust results with regard to its application in practice.

The data available do not allow to firmly infer about the feasibility, safety and effectiveness of AET for HF inpatients. However, the limited evidence demonstrates a tendency toward the positive application of exercise in clinical practice of inhospital patients with HF. Larger studies are needed with strong samples of patients and robust design of investigation.

RELEVANCE TO CLINICAL PRACTICE

The results illustrate a missing area of clinical evidence. Cardiac rehabilitation is considered for experts the most effective non-pharmacological intervention for cardiac patients and especially for HF patients. The success of the process depends on the sequential interventions that are design for a cardiac rehabilitation program; for this reason, if some of the phases are not quite developed it could jeopardize the entire process. It is urgent to develop and test AET protocols for HF inpatients in order to promote patient's functional capacity, adherence to the therapeutic regimen and consequently an improvement on their health status and quality of life.

The absence of evidence is not an obstacle but an opportunity to create knew knowledge and improve the clinical practice.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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