

Peripheral vascular insufficiency impairs functional capacity in patients with heart failure

Insuficiência vascular periférica compromete a capacidade funcional no paciente com insuficiência cardíaca

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Abstract

Introduction: Heart failure (HF) is a complex syndrome in which effort limitation is associated with deterioration of peripheral musculature. Improving survival rates among these patients have led to the appearance of cases in which other pathologies are associated with HF, such as peripheral vascular insufficiency (PVI). The combination of these two pathologies is common, with significant repercussions for affected patients. **Objective:** To compare functional limitations and quality of life between patients with HF in isolation or HF + PVI. **Method:** Twelve patients with HF+PVI were paired to 12 patients with HF in isolation. All had ejection fraction <40%. The following were conducted: 6 minute walk test (6MWT), chair test (CT), step test (ST), one repetition maximum test (1RM) and quality of life questionnaire. **Results:** The results for the 6MWT (311±27 vs. 447±29), ST (49±3 vs. 81±10) and CT (17±1 vs. 21±1) were lower in the HF+PVI group than in the HF group (p<0.05). The HF+PVI group exhibited a reduction in the number of steps taken from the first to the second minute of the ST, in relation to the HF group. The HF group exhibited better HR recovery than the HF+PVI group (50±4 vs. 26±3; p<0.05). No differences were found in results for the Borg scale, the peripheral muscle strength test (1RM) or the questionnaires (p>0.05). **Conclusions:** The study participants who had mixed disease exhibited a greater degree of functional impairment than the group with HF, without reporting worsened quality of life.

Keywords: heart failure; peripheral vascular insufficiency; quality of life; 6-minute walk test; physiotherapy.

Resumo

Introdução: A insuficiência Cardíaca (IC) é uma síndrome complexa e a limitação ao esforço está associada à piora da musculatura periférica. Devido à melhora na sobrevida destes pacientes, observa-se o surgimento de patologias associadas à IC, como a insuficiência vascular periférica (IVP). A associação das duas patologias é comum e com grandes prejuízos aos pacientes acometidos. **Objetivo:** Comparar as limitações funcionais e a qualidade de vida em IC isolada e IC + IVP. **Método:** Doze pacientes com IC+IVP foram pareados a 12 pacientes com IC isolada. Todos possuíam fração de ejeção <40%. Foram realizados: teste da caminhada de seis minutos (TC6M), teste da cadeira (TCAD), teste do degrau (TD), teste de uma repetição máxima (1RM) e questionário de qualidade de vida. **Resultados:** Os valores obtidos nos testes TC6M (311±27 vs. 447±29), TD (49±3 vs. 81±10) e TCAD (17±1 vs. 21±1) no grupo IC+IVP foram menores do que no grupo IC (p<0,05), respectivamente. O grupo IC+IVP obteve redução do número de degraus alcançados entre o primeiro e o segundo minuto do TD em relação ao grupo IC. O grupo IC apresentou melhor recuperação da FC em relação ao grupo IC+IVP (50±4 vs. 26±3; p<0,05). Não foi encontrada diferença na escala de Borg, na força muscular periférica (1RM) e nos questionários aplicados (p>0,05). **Conclusão:** No presente estudo, os participantes com doença mista apresentaram maior comprometimento funcional em relação ao grupo com IC, sem demonstrar piora na qualidade de vida.

Palavras-chave: insuficiência cardíaca; insuficiência vascular periférica; qualidade de vida; teste de caminhada de seis minutos; fisioterapia.

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■ INTRODUCTION

Heart failure (HF) is a complex clinical syndrome of a systemic nature that is the common end stage of the majority of cardiovascular diseases and is characterized by neurohumoral exacerbation, skeletal myopathy and reduced functional capacity.¹⁻⁵ It is an important public health problem with growing prevalence and hospital admission rates and is linked to high levels of morbidity and mortality.²⁻⁵ The syndrome can involve peripheral musculature and has a close relationship with exercise intolerance.⁶

With advances in medicine and drug therapies, HF is now seen in combination with other pathologies, which has an even greater negative impact on quality of life and the ability to perform daily activities. One pathology that is often found in combination with HF is peripheral vascular insufficiency (PVI),⁷ because of the many risk factors that the two pathologies have in common. In 90% of cases the reduced blood flow because of arterial obstruction has atherosclerotic origins.^{8,9} These types of obstruction are most frequently seen in the lower limbs and more than 20% of elderly populations can be affected.

The pathophysiology of PVI is related to an imbalance between circulatory delivery of nutrients and oxygen and the demand from skeletal musculature, which, in common with HF, causes functional impairment and changes to fiber types.^{10,11} The reduction in oxygen delivery is also common to both pathologies¹² and can provoke changes in muscle fiber types, while the chronic ischemic process can provoke structural and functional changes to the skeletal musculature. The compounded effects of risk factors – low cardiac output (Q_T) and peripheral arterial occlusion – can reduce oxygen delivery to the muscles still further, potentially impacting on performance of daily activities, such as walking and going up and down stairs, in addition to having a negative impact on quality of life. The objective of the present study was therefore to compare functional limitations and quality of life in patients with HF only or HF and PVI.

■ METHODS

A total of 12 patients with Peripheral Vascular Insufficiency and Heart Failure (HF+PVI Group), aged 45 to 80, were enrolled and paired for age and sex to 12 patients with HF alone (HF Group). The primary inclusion criterion for the study was sedentary patients with cardiomyopathy (ejection fraction <40%), previously confirmed by echocardiogram. Members of the HF+PVI group also had a diagnosis of unilateral or bilateral Peripheral

Arterial Occlusive Disease with limiting Intermittent Claudication (IC).

All patients were on medication optimized for HF and all members of the HF+PVI group had stable clinical status and were on specific medication for this pathology (Simvastatin, Aspirin or Ticlopidine, Cilostazol). Patients were excluded if they suffered from pain at rest and trophic lesions (Fontaine stages III and IV); had prior surgery; chronic obstructive pulmonary disease; or decompensated HF; or if their clinical condition prevented them from performing the physiotherapeutic assessment tests or osteomuscular and/or neurological diseases that prevented them from performing the tests.

Each patient was provided with an Informed Consent Form that had been approved in advance by the Ethics Committee at the Instituto Dante Pazzanese de Cardiologia (n° 9095). After they had signed the forms, patients underwent a physiotherapeutic assessment, and performed a 6-minute walk test (6MWT), a chair test (CT) a step test (ST) and one repetition maximum (1RM) tests for upper and lower limbs, and then answered the Minnesota quality of life questionnaire and an analog visual pain scale, and maximal inspiratory and expiratory pressure were measured.

Six-minute walk test (6MWT)

Tests were conducted in a 30-meter level corridor, delimited by two cones, as described by ATS criteria.¹³ Before the test, measurements were taken of arterial blood pressure (BP) (sphygmomanometer - Unilec® and stethoscope - Littmann Quality), heart rate (HR) and peripheral oxygen saturation (SpO_2) (portable oximeter– OxiPlus®) and the Modified Borg Scale of Perceived Exertion.¹⁴ The variables HR and SpO_2 were monitored continuously throughout the test. All measurements were taken again at the end of the test and after a 2-minutes recovery period.

Step test (ST)

This test was conducted using a ‘step’ with a height of 20 cm and lasted 4 minutes, during which time the participant stepped up and back down at a velocity within their own limits. During the test, the tester provide verbal encouragement, employing a constant tone of voice, with the objectives of providing both encouragement and information on the participant’s performance in the test. Heart rate and SpO_2 were measured throughout the test. Blood pressure was measured and the Borg test conducted at the start and end of the test and after a 2-minute recovery period.

Chair test

The chair test (CT) was conducted using a chair without arms. The participant was asked to sit on the center of the chair with their spine erect, feet shoulder-width apart and arms crossed across the chest and to rise and sit down as quickly as possible for one minute. The examiner recorded the number of times the participant managed to complete this movement. Heart rate and SpO₂ were measured at the start of the test, at the end of the test and after a two-minute recovery period.

Assessment of respiratory muscle strength

Maximum respiratory pressures were acquired using digital vacuum manometer (MVD-300 V.1.1 Microhard System, Globalmed, Porto Alegre, Brazil), with an operating range of ± 300 cmH₂O. For measurement of maximum inspiratory pressure (MAX_{IP}), the patient was requested to perform a maximum inspiration, starting from residual volume. For measurement of maximum expiratory pressure (MAX_{EP}), the patient was requested to perform a maximum expiration, starting from total lung capacity. Each patient performed five maximum inspirations and five maximum expirations, held for at least two seconds, the results of which had to be similar (<10% difference), and the highest result of five was used for the analysis. All results were tested against equations for prediction of normal values.¹⁵

Questionnaires

The severity of HF was quantified for both groups using the quality of life questionnaire (Minnesota).¹⁶ Additionally, the mixed group (HF+PVI) also answered the Edinburgh Claudication questionnaire, for which each patient identifies the exact location of pain. Patients also quantified pain intensity using an Analog Visual Scale – AVS.

One repetition maximum

One repetition maximum (1RM) tests were used to assess the muscle strength of lower and upper limbs. All tests were conducted on the non-dominant side and dumbbells were used for arms and ankle weights for legs.

Criteria for Termination of Tests

If any patient suffered from unbearable pain in the limb affected by PVI, HF and/or PVI decompensation, heart rate <50 bpm, dizziness, nausea, clouded vision, tingling feelings in the body, (systolic BP <80 mmHg and diastolic BP <50 mmHg)

or cold extremities, the test was terminated and the patient sent for medical examination.

STATISTICAL ANALYSIS

Initially, the Kolmogorov-Smirnov test was used to analyze data distribution. Student's *t* test and the chi-square test were used for comparisons between the HF and HF+PVI groups. Additionally, Pearson correlation coefficients were calculated for the variables analyzed. Differences were considered statistically significant if $p < 0.05$ for all analyses.

RESULTS

A total of 12 patients with HF in isolation and 12 patients with HF+PVI were analyzed, all of them in NYHA functional class II. None of the patients had pacemakers and/or implantable cardioverter-defibrillator. No differences were detected between the two groups in terms of anthropometric variables, personal histories or medication, as can be observed in Table 1.

Table 1. Characteristics of patients studied.

| | HF (n=12) | HF + PVI (n=12) |
|--------------------------|--------------|--------------------|
| Age (years) | 66 \pm 2 | 67 \pm 2 |
| Weight (kg) | 73 \pm 4 | 70 \pm 4 |
| Height (cm) | 165 \pm 2 | 164 \pm 3 |
| BMI (kg/m ²) | 26 \pm 1 | 26 \pm 1 |
| History | | |
| Ex-Smoker | 7 (58%) | 7 (58%) |
| Smoker | 0 (0%) | 3 (25%) |
| AMI | 8 (67%) | 3 (25%)* |
| SAH | 12 (100%) | 7 (58%) |
| DM | 4 (33%) | 5 (42%) |
| DLP | 10 (83%) | 10 (83%) |
| HF+CF | 2 (17%) | 6 (50%)* |
| Diagnoses | | |
| Chagas CMP | 1 (8%) | --- |
| Ischemic CMP | 8 (67%) | 10 (80%) |
| Dilated CMP | 3 (25%) | 2 (20%) |
| PVI | --- | 12 (100%) |
| Medication | | |
| B-blocker | 11 (92%) | 10 (83%) |
| Diuretic | 12 (100%) | 9 (75%) |
| ACE-I | 11 (92%) | 10 (83%) |
| Cilostazol | - | 12 (100%) |

BMI - Body Mass Index; AMI - Acute Myocardial Infarction; SAH - Systemic Arterial Hypertension; DM - Diabetes Mellitus; DLP - Dyslipidemia; HF+CF - Family History Positive for Coronary Failure; CMP - Cardiomyopathy; PVI - Peripheral Vascular Insufficiency; B-blocker - Beta Blocker; ACE-I - Angiotensin-Converting Enzyme Inhibitor. *Statistically significant difference between groups ($p < 0.05$).

Patients with mixed disease (HF+PVI) covered a significantly shorter distance in the 6MWT than patients in the HF group (Table 2). Additionally, five patients (42%) in the HF+PVI group terminated the 6MWT because of fatigue and/or pain in the lower limbs, whereas none of the patients in the HF group needed to terminate the test ($p<0.05$). It was also observed that total number of steps taken in the ST and number of repetitions in the CT were both significantly lower for the group with mixed disease. Additionally, six patients (50%) in the HF+PVI group terminated the ST because of fatigue and/or pain in the lower limbs, compared to two patients (17%) in the HF group ($p<0.05$) who terminated the step test (Table 2). Furthermore, the HF+PVI group did not only manage a lower total number of steps, but, as shown in Figure 1, these patients also exhibited a considerable reduction in the number of steps taken from the first to the second minute, reducing gradually over time, which was not observed in the group with HF in isolation.

Peak HR during the clinical tests was higher in the HF+PVI group, but the difference was not statistically significant (Table 2). Notwithstanding,

the change (Δ) in HR in the second minute of recovery (Δ HR Peak - Recovery) from the ST was significantly higher in the group with HF in isolation than in the mixed group (50 ± 4 vs. 26 ± 3 ; $p<0.05$), respectively. We also observed that Δ HR was higher in the HF only group for the 6MWT and the CT, but the differences in comparison with the HF+PVI group were not significant (Figure 2). No differences were detected between the HF and HF+PVI groups for the variables MAX_{IP} (88 ± 10 vs. 79 ± 29 , respectively) or MAX_{EP} (99 ± 14 vs. 128 ± 27 , respectively). The values of MAX_{IP} and MAX_{EP} were corrected for the percentages projected for the Brazilian population and once more no differences were found between the groups ($p>0.05$). There were also no significant

Table 2. Variables analyzed for both groups.

| | HF (n=12) | HF + PVI (n=12) |
|-----------------------------|-----------|-----------------|
| 6MWT | | |
| Distance (m) | 447±29 | 311±27* |
| Peak Borg Dyspnea | 4±1 | 3±1 |
| Peak Borg LL | 4±1 | 5±1 |
| Peak HR (bpm) | 102±3 | 105±5 |
| Test terminated | 0 | 5 (42%)* |
| Chair test | | |
| Repetitions | 21±1 | 17±1* |
| Peak Borg Dyspnea | 3±1 | 2±1 |
| Peak Borg LL | 3±1 | 3±1 |
| Peak HR (bpm) | 96±4 | 102±5 |
| Step test | | |
| Total number of steps | 81±10 | 49±3* |
| Peak Borg Dyspnea | 4±1 | 4±1 |
| Peak Borg LL | 5±2 | 7±1 |
| Peak HR (bpm) | 121±11 | 124±13 |
| Test terminated | 2 (17%) | 6 (50%)* |
| Questionnaire | | |
| Minnesota | 32±6 | 29±7 |
| Borg Scale | --- | 6±1 |
| 1 Repetition Maximum | | |
| UL (Kg) | 5±1 | 6±2 |
| LL (Kg) | 9±1 | 8±7 |

6MWT - 6-Minute Walk Test; CT - Chair Test; ST - Step Test; Borg - Modified Borg Scale; LL - Lower Limbs; UL - Upper Limbs; Kg - Kilograms; bpm - Beats Per Minute. *Statistically significant difference between groups ($p<0.05$).

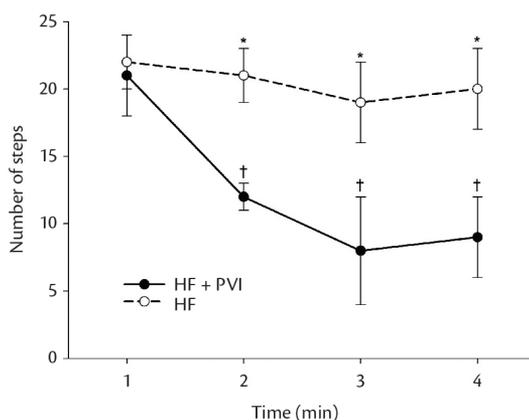


Figure 1. Comparison between groups of number of steps climbed during the test. HF Only Group (unshaded circle/broken line) and HF+PVI group (shaded circle/unbroken line). Figures are expressed as mean ± SD. Notes: * $p<0.05$; significant difference between HF and HF+PVI. † $p<0.05$; difference compared to first minute.

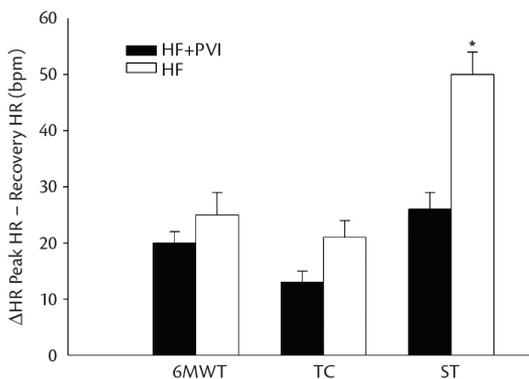


Figure 2. Comparison between HF group (unshaded bars) and HF+PVI group (shaded bars) for Δ HR (Peak HR - Recovery HR) during clinical tests. Figures are expressed as mean ± SD. Note: * $p<0.05$; significant difference between HF and HF+PVI.

differences observed for the Borg scale results at peak during the tests, for peripheral muscle strength (1RM) or for the results of questionnaires administered to both groups ($p>0.05$).

DISCUSSION

The objective of this study was to compare functional limitations and quality of life in patients with HF in isolation and patients with both HF and PVI. Patients with mixed disease (HF+PVI) had greater functional deficits, with lower results for the 6MWT, CT and ST than patients with HF in isolation. It was also observed that Δ HR (peak – recovery) was lower in the HF+PVI Group.

Some studies have suggested that the chronic ischemic process to which peripheral muscles are subjected can lead to reduced muscle strength and resistance among patients with PVI; these, in turn, tend to trigger further unfavorable mechanisms, leading to changes to the muscular phenotype.^{12,17,18} Another important factor in patients with PVI is the presence of pain in areas distal to damage caused by ischemia provoked by the pathology itself¹⁹ and, as a result, these patients tend to have lower physical activity levels and impaired walking capacity, all of which results in a general process of loss of fitness, inactivity and worsened quality-of-life.²⁰

Arterial damage may be exacerbated by the abnormal hemodynamic response, chronic venous insufficiency or heart failure; it was notable that patients with PVI achieved shorter distances in the 6MWT than patients with HF alone. Although the results for quality of life were not different between the groups, it can be observed that in the present study day-to-day activities, represented by the 6MWT, CT and ST, were impaired for patients with HF+PVI. We believe that histological abnormalities in skeletal muscle of HF patients, such as muscle atrophy and reduced mitochondrial density,²¹⁻²³ may have impacted these patients' capacity for microvascular O₂ extraction. This in turn suggests that the patients with mixed disease suffer greater musculoskeletal compromise, leading to lower tolerance of exercise, as observed in the clinical tests.

Studies have shown that ergoreflex activity is exacerbated in HF patients, meaning that they exhibit abnormal HR responses.⁵ Exacerbation of this mechanism could have caused the mixed group to reach higher peak HR during the tests than the HF group, but this effect was not observed in the present study, which was probably the result of the small number of patients. We believe that the pain provoked by arterial obstruction made a greater contribution to limitation of exercise and termination

of the tests, meaning that the cardiovascular capacity of this group was underestimated.

The greater time taken for HR to recover in patients with HF is related to increased sympathetic activity.^{24,25} The pathophysiology of PVI leads us to believe that there may also be exacerbation of ergoreflex and of sympathetic activity in these patients, indicated by the observation of elevated HR recovery time in the mixed group. Significant differences in HR variability have already been demonstrated in heart patients with PVI.²⁶ This abnormality of autonomic regulation could be interpreted as a compensatory mechanism for the reduced vasodilator capacity of arterioles seen in PVI.

According to Fick's equation [$VO_2 = Q_T \times \text{dif}(a-vO_2)$], oxygen consumption (VO_2) can be limited by the capacity to supply or by the ability to use O₂ (central mechanisms [convective] and peripheral mechanisms [diffusive]). It has already been demonstrated that the velocity with which Q_T increases is compromised in patients with HF and, as a result, O₂ supply to tissues is also reduced in these patients, further compromising peripheral musculature.²⁷ We believe that the combination of HF with PVI compromises this mechanism even further (the combination of reduced central supply and peripheral obstruction), thereby consuming all available O₂ and, probably, using anaerobic metabolic pathways to enable exercise to continue. This effect may be attenuated when drugs to promote peripheral vasodilation are used, such as, for example sildenafil.²⁸ The improvement in nitric oxide bioavailability to peripheral musculature improves the delivery/utilization imbalance during exercise and accelerates VO_2 kinetics, with positive effects on exercise tolerance in patients with HF. If we take the peripheral arterial occlusion seen in patients with HF+PVI into consideration, the possibility of endothelial dysfunction and reduced nitric oxide production would explain the reduced functional capacity observed among these patients in the present study.

LIMITATIONS TO THE STUDY

The present study suffers from certain limitations, which should be taken into consideration:

- Small number of patients;
- No validation of the step test as a method of evaluating patients with heart failure and peripheral vascular insufficiency;
- No measurement of VO_2 during the tests;
- No measurement of lactate;
- Tests not conducted in duplicate.

■ CONCLUSIONS

We conclude that the group of patients with mixed disease (HF+PVI) exhibited similar quality-of-life and muscle strength, both respiratory and peripheral, to the patients with HF in isolation. However, the mixed disease group exhibited a decline in functional capacity and in the ability to perform daily activities, when compared with the group with HF alone. Although there is scant literature on cases of HF in combination with PVI, the importance of conducting further studies to compare functional impairment between these groups of patients is clear.

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