



Interplay of cognitive functions and functional status in heart failure

Interação das funções cognitivas e do status funcional na insuficiência cardíaca

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Abstract

Background: Heart failure (HF) reduces functional status, which may be linked to cognitive decline. Understanding the impact of cognitive function is essential for disease management, as it requires significant patient comprehension to ensure effective treatment and to influence daily activities. **Aim:** To assess how episodic memory and executive function contribute to functional status in daily life activities in HF patients. **Methods:** The study used a cross-sectional design with an age-matched control group. The convenience sample consisted of patients with HF (independent of left ventricular ejection fraction) and healthy volunteers age-matched in the control group from the community. Data was collected from April to December 2018. We utilized Rey's Auditory Verbal Learning Test, Trail Making Tests (TMT A and B), Glittre Activities of Daily Living test (Glittre-ADL), and Instrumental Activities of Daily Living Scale to measure episodic memory, executive function, functional status in daily living and functional dependence, respectively. **Results:** We recruited 57 participants (HF=37; Control=20). Five HF patients were excluded because they did not complete all tests. HF patients exhibited a prolonged duration to complete the Glittre-ADL test compared to controls (287.9 ± 91.2 vs. 212.7 ± 34.9 seconds; $p < 0.001$). Episodic memory scores did not significantly differ between the groups. However, as measured by the TMT, the HF group's executive function was notably poorer. Regression analysis revealed that HF and executive function (TMT A and B) significantly impacted functional status, explaining 24.1% of the variance ($R^2 = 0.241$, $p < 0.001$). In a second regression model (HF, TMT-A, TMT-B, and age), HF ($p=0.001$) and age ($p=0.009$) were significant. The variance in the functional status was 27.3% ($R^2= 0.273$), attributable to the variables HF and age. **Conclusion:** In conclusion, our results have revealed that the compromised executive function can partly explain the decline in performance on the ADL-Glittre test in HF patients. Moreover, when age was included in the model, the performance on the ADL-Glittre test was significantly associated with both age and HF.

Keywords: Heart Failure; Activities of Daily Living; Cognition; Executive Function; Episodic Memory.

Resumo

Introdução: A insuficiência cardíaca (IC) reduz o status funcional e pode levar ao comprometimento cognitivo. Compreender o impacto da função cognitiva é essencial para o manejo da doença, pois exige uma compreensão significativa por parte do paciente para garantir um tratamento eficaz e influenciar as atividades de vida diárias. **Objetivo:** Avaliar a contribuição da memória episódica e da função executiva no status funcional das atividades da vida diária em pacientes com IC. **Métodos:** Estudo transversal com grupo controle pareado por sexo e idade. Amostra de conveniência de pacientes com IC (independente da fração de ejeção do ventrículo esquerdo) e voluntários saudáveis pareados por sexo e idade provenientes da comunidade. A coleta de dados foi de abril a dezembro de 2018. Teste de Aprendizagem Auditiva Verbal de Rey, *Trail Making Tests*, *Glittre Activities of Daily Living-test (Glittre-ADL test)* e Escala de Atividades Instrumentais de Vida Diária foram utilizados para avaliar, respectivamente, memória episódica, função executiva, status funcional nas atividades de vida diária e dependência funcional. **Resultados:** Recrutamos 57 participantes (IC=37; Controle=20). Cinco IC foram excluídos por não completarem os testes. Os pacientes com IC demoraram mais tempo para completar o *Glittre-ADL test* em comparação com o grupo controle (287.9 ± 91.2 vs. 212.7 ± 34.9 seconds; $p < 0.001$). Não houve diferença significativa no teste de memória episódica entre o grupo IC em comparação ao grupo



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controle. Porém, o desempenho no teste de função executiva foi pior no grupo IC. A análise de regressão mostrou que as variáveis IC e função executiva (Trilha A e B) influenciaram os escores do status funcional explicados em 24,1% ($R^2=0,241$, $p<0,001$). Em um segundo modelo de regressão (IC, TMT-A, TMT-B e idade), as variáveis IC ($p=0.001$) e idade ($p=0.009$) foram significativas. A variância do status funcional foi 27.3% ($R^2= 0.273$) atribuída às variáveis IC e idade. **Conclusão:** Os resultados mostram que o comprometimento da função executiva pode ser explicado, em partes, pela pior performance no *Glittre-ADL test* em pacientes com IC. Contudo, quando a idade entra no modelo, a performance no *Glittre-ADL test* foi explicada significativamente pelas variáveis idade e IC.

Palavras-chave: Insuficiência Cardíaca; Atividades Cotidianas; Cognição; Função Executiva; Memória Episódica.

INTRODUCTION

Heart failure (HF) is a chronic progressive condition that affects approximately 23 million individuals globally¹. It is a primary cause of hospitalization and is linked with significantly adverse outcomes, including heightened mortality and morbidity^{2,3}. The conceptualization of HF has evolved from a simple model of pump failure to a complex multisystem disorder, impacting not only the cardiovascular system but also the musculoskeletal, renal, neuroendocrine, and immune systems⁴. While considerable attention has been paid to these systems, the critical patient-centric comorbidities such as cognitive impairment and functional status deficits are less understood⁵.

The etiology of cognitive impairment in HF patients is often linked to reduced cerebral blood flow, which results in structural and functional brain changes⁵. Such changes are evident in the cortical and subcortical regions, particularly the frontal lobes, anterior cingulate, temporal-parietal lobes, and hippocampus^{6,7}. Cognitive dysfunction in HF, characterized by decreased attention, memory loss, psychomotor slowing, and impaired executive function, compromises patients' ability to adhere to complex treatment regimens, dietary sodium restriction, and self-care decisions, all of which are critical for survival⁸⁻¹⁰.

Furthermore, cognitive impairment is frequently associated with deficits in functional status^{11,12}. Assessing functional status is crucial in clinical settings as it reflects the severity of an individual's limitations and prognosis^{13,14}. One method to evaluate status capacity is patient observation during Activities of Daily Living (ADL). The Glittre Activities of Daily Living test (Glittre-ADL test), which simulates common everyday activities like stair climbing and object lifting, is a recognized tool for assessing functional status in HF patients^{15,16}.

Studies indicate that certain cognitive domains may predict functional status more effectively than others. However, literature is sparse when comparing the predictive value of different cognitive domains on individual functional abilities^{17,18}. Episodic memory allows an individual to recall unique, specific events. Executive function encompasses a range of cognitive skills, such as visual search, perceptual and motor skills, processing speed, attention, task-switching, and working memory. We theorize that deficiencies in

these two cognitive areas may play a role in reducing an individual's ability to perform everyday functions^{19,20}. Therefore, this study explores the influence of episodic memory and executive function on daily functional status, as assessed by the Glittre-ADL test in HF patients.

METHODS

Study design and participants

The study used a cross-sectional design with an age-matched control group. The convenience sample consisted of 37 patients with HF (independent of left ventricular ejection fraction) and 20 healthy volunteers age-matched in the control group from the community. The participants of the HF group were recruited from a Public Health Center in Southern Brazil. HF was defined according to established criteria in the European Society of Cardiology guidelines²¹. Data were collected from April to December 2018. Exclusion criteria were a history of clinical stroke and the presence of a disorder known to influence cognition, such as a diagnosis of dementia or a primary psychiatric condition, or conditions that could limit the patient's ability to complete the tests, including neuromuscular dysfunction, hemiplegia, and impaired vision or hearing.

Moreover, individuals with unstable angina, thrombophlebitis, intracardiac thrombus, or pulmonary edema and those with systolic BP higher than 160 mmHg or diastolic BP higher than 105 mmHg were excluded from the study. Written informed consent was obtained from all patients. The Research Ethics Board committee of Universidade Federal de Ciências da Saúde de Porto Alegre approved the study by protocol number 2.547.885. Patient clinical data were extracted from medical records. They included age, sex, education years (> nine years or < nine years), left ventricular ejection fraction, and functional class, according to the New York Heart Association (NYHA).

Rey's Auditory Verbal Learning Test (RAVLT)

Episodic memory refers to an individual's unique memory of a specific event, including the spatial and temporal contexts, enabling the reconstruction of experiences from the past¹⁹. RAVLT consists of 15-word lists



read aloud for the patient, who must try to recall as many words as possible (A1). The procedure is repeated four more times for the assessment of learning (A5); then, it is followed by a distractor list and by two free recalls – one immediate (A6) and one delayed (A7). The test is concluded after a recognition task (Rec), where the subject must correctly identify the words from the target list among 35 distractors. The total number of words recalled on the A1, A5, A6, and A7 trials were selected to measure memory and learning^{22,23}.

Trail Making Test (TMT)-A and B

This test evaluates the executive function and involves cognitive skills, including visual search, perceptual/motor skills, processing speed, attention, switching, and working memory. It consists of two parts: The TMT-A, which requires the subject to draw a line connecting consecutive numbers (1 to 25) randomly distributed in a sheet form, and the TMT-B, which requires the subject to alternate between numbers (1 to 13) and letters (A to M). The time (in seconds) needed for the participant to complete each task was used for analysis²⁰.

Glittre-ADL test

The Glittre-ADL test was administered to evaluate functional status, according to Fernandes-Andrade et al.²⁴. Briefly, the subjects were seated, carrying a backpack. Then, they had to walk down an aisle, with a stairway halfway through, to reach a shelf where they had to move weights from the upper shelf to the lower shelf and then to the ground. Next, they had to perform these tasks in the reverse order. The test was concluded after five cycles. The subjects were instructed to complete the test as quickly as possible and were allowed to rest during the test, but they were requested to resume it as soon as possible. The test was performed twice to avoid the learning effect, with a 30-minute interval between runs. Patients were monitored before, during, and after the tests (blood pressure, heart rate, peripheral oxygen saturation, and Modified Borg Scale by subjective perceived exertion). The total time to complete the test was registered using the best time²⁴.

Instrumental Activities of Daily Living Scale (IADL)

This scale assessed functional dependence. It was adapted to the Brazilian context and evaluated the abilities to prepare meals, do house chores, do laundry, handle money, use the telephone, self-administer medication, go shopping, and use means of transportation. The resulting scores range from 7 to 21; the lower the score, the higher the level of dependency²⁵.

Statistical analysis

Descriptive statistics for patient demographic data, NYHA, and Left ventricular ejection fraction were

determined using mean \pm standard deviation end for continuous variables and frequency for categorical variables. The distribution was tested using the Shapiro-Wilk test. Comparisons between patients with HF versus the control group were conducted using Student's t-test, chi-square tests, and Mann-Whitney. Pearson's multiple correlation test assessed the relationships between the Glittre-ADL test, executive function, episodic memory, and functional dependence. Correlation strengths were classified as very weak ($r < 0.3$), weak (0.3 - 0.46), moderate (0.5 - 0.69), strong (0.7 - 0.89), or very strong ($r > 0.9$). Using a stepwise method for variable selection, multiple linear regression was employed to explain the Glittre-ADL test performance based on variables significant in univariable analyses ($p < 0.05$). The variables included in the model were HF, Trail Making Test A and B. A subsequent regression model also incorporated age as a variable. The study's statistical power was evaluated to ensure adequate sample size. Analyses were performed using SPSS version 20.0 (IBM, Armonk, NY, USA) with a two-tailed approach; a p-value of less than 0.05 indicated statistical significance.

RESULTS

We recruited 57 participants (HF=37; Control=20). Five HF patients were excluded because they did not complete all tests. The clinical and demographic characteristics of the 52 participants are detailed in Table 1. Age and gender were similarly distributed across groups. Among patients with HF, the majority were classified as NYHA II in terms of symptom severity. The echocardiographic assessment showed that the left ventricular ejection fraction varied from 20% to 62%.

Concerning functional status, the time of execution of the Glittre-ADL test differed significantly between groups. HF patients required more time than the age-matched control group (287.9 ± 91.2 vs. 212.7 ± 34.9 seconds; $p < 0.001$), as illustrated in Figure 1.

Table 1. Clinical and demographic characteristics.

| Variable | HF group (n=32) | Control group (n=20) | p-value |
|---|--------------------|-------------------------|---------|
| Men/Women (%) | 24(75)/8(25) | 9(45)/11(55) | 0.06 |
| Age (years) | 60.2 \pm 11 | 57 \pm 13.3 | 0.36 |
| Education grade <9 years | 22 (68.7%) | 12 (60%) | 0.40 |
| New York Heart Association classes | | | |
| I | 5 (15.6%) | | |
| II | 23 (71.9%) | | |
| III | 4 (12.5%) | | |
| Left ventricular ejection fraction (%) | 37 \pm 14.5 | | |

Heart Failure = HF.

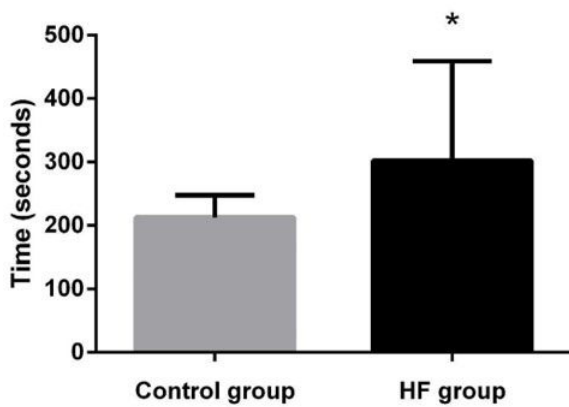


Figure 1. Glitter Activities of Daily Living test: age-matched control and heart failure (HF) groups. * $p < 0.001$ compared to the control group.

Table 2 presents the cognitive function test results. No significant difference was found in episodic memory test scores between the HF group and the control group. However, the HF group's performance on the executive function test was inferior to that of the control group ($p < 0.05$). Additionally, a disparity in functional dependence was noted; the HF group exhibited partial dependence, in contrast to the control group, which was deemed independent.

The Glitter-ADL test performance demonstrated moderate correlations with the TMT-B ($r = 0.41$; $p = 0.003$), age ($r = 0.44$; $p = 0.001$), and functional dependence ($r = 0.45$; $p = 0.001$). It also had an inverse moderate correlation with RAVLT-A6 ($r = -0.34$; $p = 0.014$). However, no significant correlation was found with the TMT-A ($r = 0.25$; $p = 0.07$), RAVLT-A1 ($r = -0.22$; $p = 0.120$), RAVLT-A5 ($r = -0.198$; $p = 0.158$), or RAVLT recognition ($r = -0.136$; $p = 0.336$). Notably, there was a significant inverse correlation with RAVLT-A7 ($r = -0.267$; $p = 0.0055$), indicating an area that warrants further investigation.

The regression analysis indicated that the variables of HF and executive function (measured by TMT-A and TMT-B) significantly influenced the functional status scores, explaining 24.1% of the variance ($R^2 = 0.241$). The power of this analysis was 91.6%. A second regression model, which included the variables HF, TMT-A, TMT-B, and age, revealed that HF ($p = 0.001$) and age ($p = 0.009$) were significant predictors. However, TMT-A and TMT-B did not show a substantial effect in this model ($p > 0.05$). This model accounted for 27.3% of the variance in functional status ($R^2 = 0.273$), and the power of the analysis was 93.3%. Further details on the regression of significant variables can be found in Table 3.

DISCUSSION

Our findings demonstrated that patients with HF have worse performance in the ADL-Glitter test, and these results may be explained, in part, by executive function. On the other hand, episodic memory does not appear to be impaired in patients with HF compared to the control group. This study is the first to illustrate an association between functional status and cognitive function, as

Table 2. Cognitive function and functional dependence.

| Variable | HF group | Control group | p-value |
|----------------|----------|---------------|---------|
| | (n=32) | (n=20) | |
| RAVLT A1 | 4.6±1.6 | 4.9±2.7 | 0.55 |
| RAVLT A5 | 9.1±2.5 | 9.1±3.4 | 0.97 |
| RAVLT A6 | 6.8±2.6 | 6.9±3 | 0.94 |
| RAVLT A7 | 6.7±2.7 | 6.6±3.1 | 0.96 |
| RAVLT Rec | 12.6±1.7 | 12.6±2.5 | 0.89 |
| Trail Making A | 67(36) | 44.5(25) | 0.01 |
| Trail Making B | 173(146) | 122.5(129) | 0.04 |
| IADL | 18(2) | 21(0) | <0.001 |

RAVLT = Rey Auditory Verbal Learning Test; RAVLT 1 = Trial 1; RAVLT 5 = Trial 5; RAVLT 6 = Trial 6 (immediate recall); RAVLT 7 = Trial 7 (delay recall trial); RAVLT Rec = RAVLT recognition trial; IADL = Instrumental Activities of Daily Living; HF=Heart Failure.

Table 3. Multiple Regression Analysis to explain the performance of Glitter Activities of Daily Living test.

| Variable | β | CI95% | p-value |
|----------------|---------|---------------|---------|
| MODEL 1 | | | |
| Groups | 58.10 | 17.65 - 98.55 | 0.006 |
| Trail Making B | 0.52 | 0.054 - 0.98 | 0.029 |
| MODEL 2 | | | |
| Groups | 64.62 | 26.8 - 103.6 | 0.001 |
| Age | 2.21 | 0.57 - 3.86 | 0.009 |

Model 1: $R^2 = 0.241$; $f^2 = 0.32$; Power= 91.6%; Model 2: $R^2 = 0.273$; $f^2 = 0.37$; Power= 93.3%.

measured by the RAVLT and TMT- A and B, and their contributions to daily living activities determined by the Glitter-ADL test in patients with HF.

Here, we found that patients with HF exhibited reduced performance in ADLs, aligning with other research showing that functional limitations in individuals with HF correlate with poorer clinical outcomes, including a higher risk of hospitalization and mortality^{26,27}. Functional limitations often render patients reliant on others for basic daily activities, like bathing and transferring, negatively impacting their quality of life²⁸. Functional status assessment is essential in clinical practice to gauge the extent of an individual's limitations and inform treatment strategies²⁹. The Glitter-ADL test offers a comprehensive evaluation involving upper and lower limb activities that mirror daily tasks²⁴, with varied physiological responses that could lead to increased cardiac overload³⁰, underscoring the value of a holistic assessment in HF patients.

Another significant finding of this study is the impairment of executive function in HF patients, corroborating prior studies linking HF to cognitive deficits^{10,14}. Executive



function is crucial for safe, independent living³¹, and HF patients often struggle with therapy adherence, decision-making, and self-care, potentially due to cognitive deficits caused by HF³²⁻³⁴. A meta-analysis revealed that 43% of HF patients experience cognitive impairment. However, estimates vary widely¹³, and cognitive impairment has been identified as a risk factor for increased mortality in HF outpatients⁵. Pressler et al. have found that deficits in memory, psychomotor speed, and executive function predict all-cause mortality within 12 months of HF outpatients¹⁰.

In contrast, we did not observe differences in episodic memory between HF patients and controls, suggesting that while memory is necessary for ADL performance, it is not solely indicative of functional independence^{11,18}. Our findings emphasize the predictive value of cognitive testing for functional status and support research identifying executive function as a significant correlate of ADL performance in older adults^{18,35}. Recognizing the concurrence of executive decline and ADL dependence could guide the intensification of supervision and care for patients.

Functional status appears to be a marker of visuospatial and executive abilities. Those with functional dependence are more susceptible to external distractions and reliant on external support, lacking an internal reference frame and more easily disoriented by changing environments. Conversely, independent individuals can better construct a comprehensive environmental representation^{27,28}. Our regression analysis supports a connection between HF, age, cognitive function, and functional status, explaining 24,1% of the variance in functional status. These findings resonate with Royall et al.'s report of a 21% average variance in functional outcomes accounted for by cognitive function¹⁸. Our results also concur with the established link between cognitive impairment and ADL dependence documented in the literature^{36,37}.

We acknowledge that this study has limitations. This is a single-center study with a small sample size. We only used episodic memory and executive function in this study. We believe that further studies should use other cognitive domains and verify their contribution to the functional capacity of ADLs.

The study highlights the need for health professionals to consider assessing and treating functional status and cognitive function in HF. We believe that the assessment of cognitive function should be part of health treatment. This integrated approach will ensure a more thorough evaluation, facilitating the creation of personalized interventions to enhance daily functioning and quality of life for individuals living with HF.

CONCLUSIONS

In conclusion, our results have indicated that compromised executive function partially accounts for the observed decline in ADL-Glittre test performance among

patients with HF. Moreover, when age was included in the model, the performance on the ADL-Glittre test was significantly associated with both age and HF.

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CONFLICT OF INTEREST

None

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