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Evaluation of cognitive Function in Elderly patients hospitalized for Heart Failure with and without Diabetes Mellitus

Avaliação da função cognitiva em pacientes idosos hospitalizados por insuficiência cardíaca com e sem diabetes melitos

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RESUMO

Pacientes idosos com diabetes melitus (DM) hospitalizados por insuficiência cardíaca (IC) apresentam frequentemente sinais de comprometimento cognitivo (CC). **Objetivo:** Avaliar a função cognitiva de idosos portadores de IC com e sem DM. **Métodos:** Pacientes hospitalizados (≥ 65 anos) por IC foram avaliados através de testes cognitivos: Montreal Cognitive Assessment (MoCA) e Mini-Cog. **Resultados:**196 pacientes, com média de idade de 73,04 ± 6,04. Segundo o Mini-cog, 77% tinham CC. O escore médio do MoCA foi de 14,60 ± 5,79. De acordo com presença ou ausência de DM, foi observado associação significativa com o sexo, feminino 54,7% vs masculino 45,3% (p=0,04) e cintura abdominal, aumentada 81,3% vs normal 18,8% (p=0,02). No cenário de cognição normal pelo Mini-cog, pacientes com pré-diabetes tinham maior probabilidade de ter fração de ejeção do ventrículo esquerdo (FEVE) normal (60,75 ± 11,15) em comparação com pacientes com diabetes (47,00 ± 14,42) e pacientes euglicêmicos (44,50 ± 19,92), p = 0,035. **Conclusão:** Foi encontrado elevada frequência de CC em pacientes idosos hospitalizados por IC. Pacientes com pré-diabetes sem CC tiveram maior probabilidade de apresentar FEVE preservada.

Palavras-chave: Insuficiência Cardíaca; Idoso; Cognição; Diabetes

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ABSTRACT

Elderly patients with diabetes mellitus (DM) hospitalized for heart failure (HF) often show signs of cognitive impairments (CI). **Objective:** To evaluate the cognitive function of elderly people with HF both with and without diabetes. **Methods:** Hospitalized patients (≥ 65 years) with HF were evaluated using cognitive tests: Montreal Cognitive Assessment (MoCA) and the Mini-Cog. **Results:** Studied 196 consecutive patients, mean age was 73.04 ± 6.04. According to Mini-cog, 77% had CI. The mean MoCA was 14.60 ± 5.79. The assessment of the clinical profile with the presence or absence of DM, showed a significant association with gender, female 54.7% vs male 45.3% (p=0.04) and waist classification, high 81.3% vs normal 18.8% (p=0.02).In the setting of normal cognition by Mini-cog, prediabetes patients were more likely to have normal left ventricular ejection fraction (60.75 ± 11.15) in comparison with diabetes (47.00 ± 14.42) and normal glucose tolerance patients (44.50 ± 19.92), p=0.035. **Conclusion:** We found a high frequency of cognitive impairment in elderly patients hospitalized with heart failure. Patient with prediabetes without cognitive impairment were more likely to have preserved ventricular function.

Keywords: Heart Failure; Elderly; Cognition; Diabetes

INTRODUCTION

Heart failure (HF) is a multidimensional syndrome with a variety of signs and symptoms associated with functional and structural cardiac abnormalities, with a high prevalence in the geriatric population (Hanon et al. 2021). Some studies have demonstrated that patients hospitalized for HF may show signs of cognitive impairments in executive functions, memory, speech, and mental processing speed (Holm et al. 2020)

Among the comorbidities associated with HF that influence prognosis, the presence of diabetes is highlighted (Basile et al. 2013). Several factors participate in the pathophysiology of diabetes in the geriatric population. Advanced age leads to the exacerbation of chronic systemic inflammation, oxidative stress, DNA damage, decline in mitochondrial function, cellular senescence and tissue dysfunction, conditions that contribute to generating metabolic disorders (Yosef et al. 2023).

The Montreal Cognitive Assessment (MoCA) is a simple tool that allows you to determine whether there is impairment in cognitive function, including the ability to understand, reason and remember.

The Mini-Cog represents another instrument for cognitive assessment, which is quick to perform and can provide additive prognostic information along with pre-existing prognostic factors for heart failure (Saito et al. 2020, Hs et al. 2016).

The objective of this study is to evaluate the cognitive function of elderly patients hospitalized according to the presence of diabetes.

STUDY POPULATION AND METHODS

We conducted a cross-sectional study of analytical nature. Studied 196 consecutive patients admitted to the cardiology ward with symptomatic HF. The following exclusion criteria was considered: those with a clinical diagnosis of HF without the echocardiographic criteria, and patients with clinical instability (neurological and/or hemodynamic) that would compromise the application of the research instruments as well as the performance of complementary exams.

For the diagnosis of DM, hemoglobin A1C (HbA1c) of 6.5% or greater was used, and for pre-diabetes between 5.7 and 6.4% (Colagiuri 2021).

Heart failure was classified according to ejection *fraction (EF) as: reduced left ventricular EF (LVrEF)* ≤ 40%, mildly reduced left ventricular EF (LVmrEF) 41-49% and preserved left ventricular EF (LVpEF) ≥50%. Echocardiograms were performed within the first fifteen days of hospital admission. LVEF was obtained from apical two and four chamber views and calculated using the Simpson method.

In the MoCA cognitive performance was rated from 0 to 30 points. In the present study, a score below 26 points was considered as cognitive impairment (Carson et al. 2018). The Mini-Cog was performed as a quick cognitive screening test with a total score of 5 points. (Normal results: 3 to 5 points, and abnormal results: 0 to 2 points) (Borson et al, 2003).

Statistical analysis

Quantitative variables were described by means ± standard deviation (SD) statistics for parametric variables and non-parametric variables were described as medians, minimum and maximum values. To compare groups based on categorical variables or proportions, we used Pearson's chi-square test or Fisher's exact test, where appropriate, with a 5% significance level. Analyzes were performed using the Statistical Package for the Social Sciences, version 23 (SPSS Inc., Chicago, Illinois, USA). A p-value less than 0.05 was considered statistically significant.

Ethical considerations

The principles of the Declaration of Helsinki of the World Medical Association were considered. The protocol was approved by the Institutional Ethic in Research Review Board (CAAE 21885019.4.0000.5197, in compliance with Resolution 466/12 of the National Health Council

RESULTS

Table 1 shows the main characteristics of the study patients. Age ranged from 65 to 96 years, mean 73.04 SD ± 6.04, where more than 50% between 70 and 79 years. 53.6% were male.

Table 1 – Clinical characteristics of the study patients

	n (%)
	196 (100.0)
Age (years)	
65 a 69	65 (33.2)
70 a 79	105(53.6)
80 a 96	26 (13.3)
Sex	
Male	105(53.6)
Female	91 (46.4)
WC (cm)	
High	86 (43.9)
Normal	33 (16.8)
HbA1c test	
Diabetes	86 (43.9)
Pre-diabetes	49 (25.0)
Normal	46 (23.5)

BMI – body mass index; WC- waist circumference; CAD –coronary artery disease HbA1c: glycosylated hemoglobin

Diabetes was present in 44% of patients, 88% had hypertension 52% had chronic obstructive pulmonary disease, 17% and 50% chronic kidney disease (assessed by the glomerular filtration rate using the Chronic Kidney Disease Epidemiology Collaboration -CKD-EPI).

Regarding the LVEF classification, 40.3% of patients had HFrEF; 12.2% HFmrEF and 45.9% HFpEF, with a mean LVEF of 46.6 ± 15.3%. In view of the evaluation of

clinical and cardiometabolic characteristics according to the LVEF classification, a statistically significant association was found regarding sex (p = 0.014), where a higher frequency of reduced LVEF (62%) and mildly reduced LVEF (66%) was found in males. LVpEF was found most frequently in females (58%), table 2.

Table 2 Baseline characteristics according LVEF

	LVEF				
	Reduced	Mildly reduced	Preserved		
	n (%)	n (%)	n (%)	n (%)	
Age (years)					p = 0,520
65 a 69	28 (35,4)	8 (33,3)	27 (30,0)	63 (32,6)	
70 a 79	44 (55,7)	11 (45,8)	49 (54,4)	104 (53,9)	
80 a 96	7 (8,9)	5 (20,8)	14 (15,6)	26 (13,5)	
TOTAL	**79 (100,0)**	**24 (100,0)**	**90 (100,0)**	**193 (100,0)**	
Sexo					p = 0,014
Male	49 (62,0)	16 (66,7)	38 (42,2)	103 (53,4)	
Female	30 (38,0)	8 (33,3)	52 (57,8)	90 (46,6)	
TOTAL	**79 (100,0)**	**24 (100,0)**	**90 (100,0)**	**193 (100,0)**	

LVEF - Left ventricular ejection fraction.

Table 3 Baseline characteristics according to glycemic status

	Diabetes n (%)	**Prediabetes** n (%)	**Euglicemic** n (%)	**Total** n (%)	**P**
Age (years)					p= 0.207
65 a 69	36 (41.9)	15 (30.6)	12 (26.1)	63 (34.8)	
70 a 79	44 (51.2)	26 (53.1)	29 (63.0)	99 (54.7)	
80 a 96	6 (7.0)	8 (16.3)	5 (10.9)	19 (10.5)	
TOTAL	**86 (100.0)**	**49 (100.0)**	**46 (100.0)**	**181 (100.0)**	
Sex					p =0.048
Male	39 (45.3)	33 (67.3)	25 (54.3)	97 (53.6)	
Female	47 (54.7)	16 (32.7)	21 (45.7)	84 (46.4)	
TOTAL	**86 (100.0)**	**49 (100.0)**	**46 (100.0)**	**181 (100.0)**	
WC (cm)					p= 0.022
High	39 (81.3)	17 (53.1)	21 (75.0)	77 (71.3)	
Normal	9 (18.8)	15 (46.9)	7 (25.0)	31 (28.7)	
TOTAL	**48 (100.0)**	**32 (100,0)**	**28 (100.0)**	**108 (100.0)**	
SBP (mmHg)					p= 0.017
High	30 (35.3)	8 (17.0)	7 (15.9)	45 (25.6)	
Normal	55 (64.7)	39 (83.0)	37 (84.1)	131 (74.4)	
TOTAL	**85 (100.0)**	**47 (100.0)**	**44 (100.0)**	**176 (100.0)**	
MINI-COG					p = 0.379
Cognitive impairment	62 (74.7)	41 (83.7)	38 (82.6)	141 (79.2)	
Cognitively normal	21 (25.3)	8 (16.3)	8 (17.4)	37 (20.8)	

TOTAL	**83 (100.0)**	**49 (100.0)**	**46 (100.0)**	**178 (100.0)**	
LVEF					p = 0.788
Reduced	37 (43.5)	17 (36.2)	17 (37.0)	71 (39.9)	
Mildly reduced	8 (9.4)	7 (14.9)	7 (15.2)	22 (12.4)	
Preserved	40 (47.1)	23 (48.9)	22 (47.8)	85 (47.8)	
TOTAL	**85 (100.0)**	**47 (100.0)**	**46 (100.0)**	**178 (100.0)**	

BMI – body mass index; WC- waist circumference; HbA1c: glycosylated hemoglobin; SBP- Systolic blood pressure; LVEF - Left ventricular ejection fraction

Regarding glycemic status, 43.9% had DM; 21.4% were prediabetic and 23.5% were euglycemic. The mean HbA1c was 6.9 ± 1.8%, ranged 4.6% and 15% (Table 3). There were statistically significant association between the presence of diabetes and female sex 54.7% 45.3% (p=004), higher waist circumference 81.3% vs 18.8% (p=0.02) and systolic blood pressure normal 64.7% vs high 35.3% (p=0.01). No statistically significant association was found between the presence of DM and cognitive impairment (using the Mini-cog), p= 0.37.

The Body Mass Index (BMI) by Lipschitz (kg/m^2) showed the following profile: low weight 43.9%, normal weight 16.8% and overweight/obesity 39.3%. Among the 165 patients evaluated, the mean BMI was 26.57 ± 3.99 kg/m^2

In the assessment of cognitive function, according to data from 192 patients who underwent the Mini-cog, 77% had cognitive deficits. Among the 165 patients evaluated by MoCA instrument, only 5 patients had a score ≥ 26 (table 4). The mean MoCA scale score was 14.60 ± 5.79.

Statistics for LVEF and Mini-cog classifications according to the presence or absence of DM2 are described in the table. 3. In the setting of normal cognition by Mini-cog, pre-diabetes patients were more likely to have normal LVEF (60.75 ± 11.15) in comparison with diabetes (47.00 ± 14.42) and normal glucose tolerance patients (44.50 ± 19.92), p=0.035

Table 4. LVEF acoording to cognition (Mini-cog) and glycemic status.

Mini-cog	**Diabetes** Mean ± SD (P25; P75)	**Prediabetes** Mean± SD (P25; P75)	**Normal** Mean ± SD (P25; P75)	**P**
Cognitive impairment	46.08 ± 14.72 45.00 (34.50; 60.00) (n = 61)	47.00 ± 14.42 45.00 (34.00; 60.00) (n = 39)	47.53 ± 14.53 49.50 (34.00; 58.75) (n = 38)	p = 0.868
Cognitively normal	44.81 ± 17.15 50.00 (30.50; 58.50) (n = 21)	60.75 ± 11.15 63.00 (59.25; 65.50) (n = 8)	44.50 ± 19.92 34.00 (27.75; 66.50) (n = 8)	p = 0.035
P	p = 0.827	p = 0.016	p = 0.619	

DISCUSSION

Results of the evaluation of clinical and cardiometabolic characteristics, according to the LVEF classification, showed a higher frequency of reduced and mildly reduced LVEF in males. In females, preserved LVEF was found more frequently, and this agrees with data from a multicenter study (Grupper et al. 2022). Previous studies have shown that prediabetic adults, insulin resistance is associated with impaired left ventricular diastolic function, and

this association appears to be independent of blood pressure, ventricular geometry, glucose tolerance status, total plasma lipids and obesity (Sliem et al. 2011). Our findings of an association between glycemic status, LVEF and CI shows that patient with prediabetes without cognitive impairment were more likely to have preserved ventricular function.

There is limited evidence on the association between the metabolic syndrome and dementia in the elderly. Despite these well-established associations with DM, far less is known about the effects of its precursor condition, prediabetes, on brain health and cognitive function. The impact of prediabetes on the brain is of great public health significance considering that half of adults aged 60 and older are estimated to have prediabetes (Luchsinger 2010). The analysis of cognitive assessment among diabetics and prediabetics generally shows worse cognitive test results and more prevalent cardiovascular risk factors in the prediabetes and diabetes categories, when compared to patients with normal blood glucose levels (Dybjer et al. 2018). In the present study, we analyzed glycemia profile: diabetic, prediabetic and normoglycemic in relation to LVEF. In relation to gender, applying the Mini-cog as a cognitive screening instrument, no significant difference was found, however, when evaluating those without cognitive impairment, a slight trend towards better results in men was observed.

The MoCA test was developed as a screening test for mild cognitive impairment (MCI) with a cutoff of 26 (Carson et al. 2018). Studies have shown that this test has high accuracy for MCI and mild dementia in individuals with a high standard of living and more than 12 years of education (Freitas et al,2013; Malek-Ahmadi et al. 2015). Other studies already point out that age and education have an impact on the results of the cognitive screening test, and that the addition of one point to the MoCA result for those with less than 12 years of education may be sufficient for the adjustment. In this sample, only 5 patients had a score considered normal (cutoff point ≥ 26). The patients' mean MoCA scale score was low. Epidemiological data from another study carried out in Brazil showed that the MoCA test did not have high accuracy in detecting cognitive impairment without dementia in a population with low education, like the data found in the present study (only two patients with more than 12 years of education) (Cesar et al. 2019). This result was also demonstrated in the MoCA validation study in the Turkish population, where lack of education was reported as a risk factor for cognitive dysfunction (Ozdilek et al. 2014).

An important study determined the association between diabetes status, glycemia, and cognitive function among a national U.S. sample of older adults in the 2011–2014 National Health and Nutrition Examinations Surveys. They suggested that dysglycemia, as measured by HbA1c, is strongly associated with a measure of global cognitive function regardless of other factors that may affect cognition (Casagrande et al. 2021).

The limitation in this study design is the relatively small sample size and the large proportion of the sample had a very low level of education.

CONCLUSIONS

We found a high frequency of cognitive impairment in elderly patients hospitalized with heart failure. Patient with pre-diabetes without cognitive impairment were more likely to have preserved ventricular function. The analysis of cognitive function and glycemia status, according to Mini-cog, demonstrated a statistically significant association in the prediabetic elderly category. These had lower LVEF when the cognitive screening instrument was compatible with cognitive disorder.

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