Frailty in Portuguese Heart Failure Patients: - a phenotype that transcends age

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Background and Aims

Frailty phenotype (FP) is a state of reduced ability to respond to external stressors due to a lack of functional and nutritional reserves. It is defined by the presence of three from the following five clinical features: **weakness, slow walking speed, unintentional weight loss, exhaustion, and low physical activity** [1]. Frailty is very common in **heart failure** (HF) patients, with prevalences ranging from 14% in the community to 77% in hospitalized individuals [2]. Older adults with concomitant FP and HF are at **increased risk of poor clinical outcomes**, early disability, hospitalization and long-term mortality [3,4]. In a recent study, this research group described FP in a sample of Portuguese HF outpatients (n = 136, 34% women, 24-81 years, 15.4% frail), reporting a frequency of 8.1% of frail individuals below 65 years old [5]. Exceptions made to the critically ill, there is a general lack of studies on younger populations with concomitant HF and FP. As frailty has been classically regarded as a geriatric condition, these **younger patients could easily be overlooked**.

This work aims to describe differences between younger (<65 years) and older (≥65 years) pre-frail and frail HF outpatients in regard to their nutritional, functional and clinical statuses.

Methods

In this **cross-sectional study**, a sample of **HF frail and pre-frail patients** was recruited from a HF outpatients' clinic in Northern Portugal. FP was assessed and classified according to Fried et al. [1]. Muscle mass was estimated from mid-upper arm muscle circumference. Weight status was assessed using body mass index. Hand grip strength (HGS) and gait speed (GS) were measured. GS was adjusted for standing height. Medical records were reviewed. Association between participants' characteristics and age was calculated using binary logistic regression.

Results

A total of **99 patients with concomitant frailty, pre-frailty and heart failure** was enrolled in this study. The characteristics of the participants are described in **Table 1**. Women amount to 38.4% of the sample. Age ranged from 24 to 81 years. Median age was 60.0 (lower quartile: 50.0; upper quartile: 69.0) years. Pre-frail and frail participants comprise 78.8% and 21.2% of the sample, respectively, and 59.6% of the sample is younger than 65 years.

Older (≥65 years) **and younger** (<65 years) **pre-frail and frail patients were rather similar in sociodemographic, clinical and nutritional characteristics**. Notable differences regard a higher frequency of diabetes and polypharmacy in older pre-frail participants. Also, mean HGS and median GSAH were significantly higher in younger pre-frail individuals. In frail individuals, only school attendance and hand grip strength were significantly lower in older participants.

Regarding the regression models (**Table 2**), **older age was only associated with lower hand grip strength** (OR = 0.90), **slower gait speed** (OR = 0.01) **and diabetes** (OR = 4.95). Obesity, muscle mass or HF functional classes were not associated with age categories.

Discussion and Conclusions

This study compares, for the first time, older and younger heart failure patients with concomitant frailty phenotype.

The most interesting results regards a **general lack of significant effect of age on various characteristics in HF patients with FP.** Taking into consideration that our study portrays a wide range of ages and nearly 60% of participants are younger than 65 years old, age-related comorbidities would eventually play a major role in differentiating younger and older participants, if not for the fact the entire population in analysis is affected by frailty and pre-frailty. **This alone is enough to recommend the assessment of FP in all HF patients, regardless of age**.

This lack of differentiation is noticed even at the HF severity level: **being symptomatic with reduced physical exercise tolerance** (NYHA Classes II+III) **did not predict being older**.

Low **hand grip strength** is a good predictor of older age and can potentially help differentiate younger individuals with accelerated myopathy, but studies regarding hand grip strength on HF populations are needed in order to establish cut-offs associated with the progression of FP, especially regarding the onset of impaired muscle strength at younger ages.

Results (cont.)

Table 1.: Characteristics of the sample, stratified by frailty phenotype and age categories

	Pre-frail (n=78)			**Frail** (n=21)		
	<65 (n=48)	**≥65** (n=30)	***p***	**<65** (n=11)	**≥65** (n=10)	***p***
Women	16 (33.3)	9 (30.0)	0.759	5 (45.5)	8 (80.0)	0.183
School attendance			**0.016**			**0.000**
≤ 4 years	10 (20.8)	14 (46.7)		2 (18.2)	10 (100.0)	
> 4 years	38 (79.2)	16 (53.3)		9 (81.8)	0 (0.0)	
HF aetiology			0.614			0.330
Dilated cardiomyopathy	25 (54.3)	17 (58.6)		1 (10.0)	5 (55.6)	
Ischaemic	15 (32.6)	12 (41.4)		2 (20.0)	1 (11.1)	
Myocarditis	2 (4.3)	0 (0.0)		1 (10.0)	0 (0.0)	
Hypertrophic	2 (4.3)	0 (0.0)		4 (40.0)	2 (22.2)	
Others	2 (4.3)	0 (0.0)		2 (20.0)	1 (11.1)	
LVEF, %	36.3±12.3	38.1±14.2	0.554	41.1±16.6	41.3±20.1	0.971
NYHA functional class			0.500			0.261
Class I	14 (30.4)	11 (36.7)		1 (9.1)	1 (10.0)	
Class II	26 (56.5)	13 (43.3)		4 (36.4)	7 (70.0)	
Class III	6 (13.0)	6 (20.0)		6 (54.5)	2 (20.0)	
Incidental stroke	11 (23.9)	10 (33.3)	0.369	2 (20.0)	1 (10.0)	0.998
Atrial fibrillation	6 (13.0)	6 (21.4)	0.343	3 (27.3)	3 (30.0)	0.999
Diabetes mellitus	13 (27.7)	16 (53.3)	**0.023**	1 (9.1)	4 (40.0)	0.149
Polipharmacy	34 (72.3)	28 (93.3)	**0.037**	8 (72.7)	9 (90.0)	0.453
Smoking habits	22 (68.8)	10 (33.3)	0.242	4 (36.4)	0 (0.0)	0.090
Weight, Kg	79.4 [71.6, 89.7]	74.3 [68.3, 81.9]	0.170	79.3±15.2	70.9±12.2	0.183
Standing height, cm	164.9±9.2	161.9±8.2	0.138	164.3±13.5	154.2±9.0	0.062
Body Mass Index, Kg.m^{-2}	29.4±5.0	29.0±3.8	0.673	29.3±3.8	29.8±4.7	0.764
Body Mass Index Classes			0.489			0.630
Underweight + Normal	11 (22.9)	4 (13.3)		1 (9.1)	3 (30.0)	
Overweight	16 (33.3)	13 (43.3)		5 (45.5)	3 (30.0)	
Obese	21 (43.8)	13 (43.3)		5 (45.5)	4 (40.0)	
Calf circumference, cm	37.5±3.0	36.3±2.8	0.067	36.2±3.2	36.9±4.1	0.660
Tricipital Skinfold, mm	16.7 [12.3, 24.9]	15.2 [11.2, 21.3]	0.295	20.1±7.0	21.2±7.6	0.738
MAMC, cm	25.3±3.6	24.3±2.3	0.211	23.8±3.5	23.2±2.9	0.662
Handgrip Strength, Kgf	31.1±9.2	26.6±6.8	**0.021**	25.4±8.0	19.0±5.1	**0.043**
Gait Speed, m/s	0.69 [0.59, 0.86]	0.58 [0.53, 0.76]	**0.022**	0.62 [0.42, 0.72]	0.50 [0.45, 0.53]	0.181

Categorical values are presented as: number (percentage). Normally distributed values are presented as: Mean ± Standard Deviation; Values with skewed distribution are presented as: Median [Percentile 25, Percentile 75]. HF = Heart Failure; LVEF = Left Ventricular Ejection Fraction; NYHA = New York Heart Association functional HF classes. MAMC = Mid-upper Arm Muscle Circumference. Missing values: LVEF n = 9; NYHA n = 2; Incidental stroke n = 2; Atrial fibrillation n = 5; Type 2 Diabetes Mellitus n = 1; Smoking habits n = 2. Polypharmacy defined as the daily use of 5 or more medicines.

Table 2.: Results from the binary logistic regression analysis regarding age categories (<65 years and ≥65 years) for pre-frail and frail individuals

	Women		**Men**		**All**	
	OR(95%CI)	***p***	**OR(95%CI)**	***p***	**OR(95%CI)**	***p***
Handgrip Strength	0.69(0.52-0.93)	0.015	0.90(0.81-1.00)	0.060	0.90(0.83-0.98)	0.013
Gait Speed	0.01(0.00-1.24)	0.059	0.03(0.00-2.82)	0.128	0.01(0.00-0.22)	0.004
MAMC	1.23(0.77-1.96)	0.392	0.84(0.59-1.18)	0.317	1.06(0.86-1.31)	0.595
Body Mass Index						
<30 Kg.m-2	1		1		1	
≥30 Kg.m^{-2}	5.8(0.33-101.28)	0.226	0.82(0.15-4.56)	0.824	0.73(0.24-2.24)	0.577
Diabetes						
Non-diabetic	1		1		1	
Diabetic	16.19(0.39-667.98)	0.142	2.89(0.71-11.86)	0.140	4.95(1.64-14.93)	0.004
NYHA Functional Class						
Class I	1		1		1	
Class II+III	0.81(0.06-11.79)	0.880	0.32(0.08-1.37)	0.125	0.40(0.13-1.23)	0.110

Results presented in odds ratio (OR) and respective 95% confidence intervals (95%CI). MAMC = Mid-upper Arm Muscle Circumference; NYHA = New York Heart Association.

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