# **Research Letter**





# **Specific Activity Scale Improves the Detection of Symptomatic Chronic Heart Failure Patients**

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#### Introduction

Heart failure (HF) is a highly prevalent, complex clinical syndrome, that is associated with significant morbidity and mortality. HF severity can be estimated by the New York Heart Association (NYHA) classification, however, this has several limitations, including high subjectivity, poor reproducibility, and poor correlation with objective physical capacity measures. Recent studies have suggested limitations of the NYHA classification in differentiating asymptomatic patients, with NYHA functional class (FC) I from patients with mild symptoms. 4.5

The Specific Activity Scale (SAS) is an alternative method to measure functional capacity, by measuring the capacity of patients in performing activities with known oxygen consumption. This method has potentially higher reproducibility and more accurate characterization of physical restriction of HF patients.<sup>3,6</sup>

The present study aims to comparatively analyze the FC of patients with HF and reduced left ventricular ejection fraction (LVEF) determined by the NYHA system and by the SAS, correlating it with the objective measurement of physical capacity by cardiopulmonary exercise testing (CPET). In addition, we tested the hypothesis that SAS is more accurate in identifying symptomatic patients among those initially considered asymptomatic with NYHA FC I.

#### Methods

Adult patients of both sexes, with stable HF and reduced or mildly reduced (<50%) LVEF were included. Patients with comorbidities that limited physical capacity, acute diseases or hospital admission in the 12 weeks prior to the assessment were excluded.

In the same session, patients were sequentially evaluated for: 1) NYHA FC; 2) FC by the SAS method; 3) CPET with measurement of maximum volume of oxygen consumed during maximal exercise (peak VO<sub>2</sub>). All evaluations were conducted by blinded, independent, trained observers.

# **Keywords**

Heart Failure; Exercise Test; Functional Class.

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#### Statistical analysis

Continuous variables were described using mean and standard deviation and nominal variables using absolute frequency (n) and percentage (%). The chi-square test was used to assess heterogeneity of proportion distribution.

For simultaneous comparison of multiple means, we used the multivariate ANOVA, followed by the Tukey-Kramer test.

To evaluate whether the SAS method correctly classify as symptomatic those patients previously considered as NYHA FC I (asymptomatic or without functional limitation), we used the Net Reclassification Index (NRI) taking the FC assessed by CPET as the gold standard. Statistical analysis was conducted using the GraphPad Prism software, version 9.0. The level of significance was set at 5% (two-tailed p < 0.05).

#### Results

A total of 101 patients were included, with a mean age 56.3 years, 42% women. Mean LVEF was 29.2±2%; 98% of patients used beta-blockers, 89.1% angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, 9.9% used sacubitril/valsartan, and 74.6% spironolactone. The main etiologies were idiopathic (29.7%), ischemic (27.7%), and hypertensive (19.8%).

# Cardiopulmonary exercise testing

Mean peak  $VO_2$  was  $15.7 \pm 5.3$  mL/Kg/min, indicating a significant reduction in physical capacity in the studied population, despite a high scattering of values ranging from 7.1 to 38.7mL/Kg/min.

# Functional classes according to NYHA and SAS

There were significant differences in the proportion of patients in each FC assessed by different methods (Table 1). We found a higher proportion of patients with FC I assessed by the NYHA classification (24%) than by the SAS (7%) or CPET (6%), p<0.0001.

There were differences in peak  $VO_2$  between the groups classified by the NYHA (p=0,023, ANOVA), with statistically significant difference between FC I and FC III (p<0.05, Tukey-Kramer post hoc test), but not between FC I and FC II. Using the SAS, significant differences were found in peak  $VO_2$  between the different FCs (p=0.0034), with significant differences between FC I and FC II groups, and between FC I and FC III (p<0.05, Tukey-Kramer post hoc test) (Table 2, Figure 1).

Twenty-four patients (24%) were initially classified as CF I by the NYHA system, and a significantly lower number of patients (n=6, 6%) were classified as FC I by the SAS (McNemar test, p=0.00002). Therefore, 18 patients were reclassified as FC II

Table 1 – Distribution of patients by functional capacity assessed by the New York Heart Association (NYHA) classification, the Specific Activity Scale (SAS) and the cardiopulmonary exercise testing (CPET)

Functional class	NYHA	SAS	CPET	р
1	24 (24%)	7 (7%)	6 (6%)	<0.0001
II	48 (47%)	52 (51%)	24 (24%)	
III	27 (27%)	40 (40%)	62 (61%)	
IV	2 (2%)	2 (2%)	9 (9%)	

Table 2 – Peak VO2 (mL/Kg/min) by patient functional class (FC) assessed by the New York Heart Association (NYHA) classification and the Specific Activity Scale (SAS)

	FC I	FC II	FC III	FC IV	p ANOVA
NYHA	18.4 ± 7.2	15.7 ± 4.1	14.0 ± 4.2*	14.0 ± 2.9	0.0234
SAS	22.5 ± 8.1	15.8 ± 4.5*	14.9 ± 4.7*	15.0 ± 4.5	0.0034

<sup>\*</sup>p<0.05 compared with patients with functional class I.

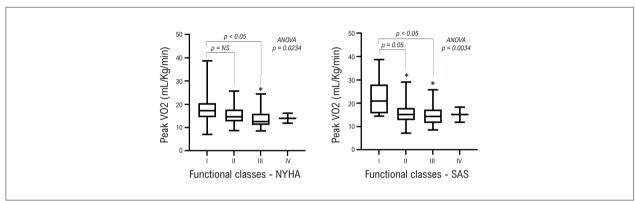


Figure 1 – Box plots illustrating peak VO2 values of the studied patients, by functional class determined by the New York Heart Association (NYHA) classification and the Specific Activity Scale (SAS). \* = p < 0.05, Tukey-Kramer post hoc test.

(50%) and FC III (50%), and 16 (89%) of these were concordant with the CPET results.

# **Discussion**

The main finding of the present study is that the use of the NYHA classification in outpatients with stable HFrEF overestimates the proportion of asymptomatic (FC I) patients, as compared with a more objective measurement of physical capacity (CPET).

The limitation of the NYHA classification in differentiating patients with mild symptoms from those actually symptomatic is reinforced by similar peak VO<sub>2</sub> values between patients with NYHA FCs I and II, in contrast with what was observed for SAS in which these values were significantly different.

These results corroborate recent studies showing that patients with NYHA FC I and FC II present an extensive overlapping of clinical severity indicators and levels of N-terminal pro-brain natriuretic peptide, suggesting that the NYHA classification does not make a clear distinction between patients with these FCs.<sup>5</sup>

In addition, we observed that SAS had a better performance in reclassifying those patients initially considered asymptomatic by the NYHA classification. The superior performance of the SAS in identifying patients with function restriction, although subtle, has important implications for the clinical practice. Persistence of symptoms has been a criterion used in several guidelines as an indication for drug treatment optimization and cardiac resynchronization therapy, aiming at reducing disease progression and increasing HFrEF patient survival.¹ Thus, our results indicate that the SAS could identify, in a cohort of outpatients with HFrEF, approximately 18% of patients who were believed to be asymptomatic using the NYHA classification, but who actually exhibited functional impairment and were candidates for treatment optimization.¹

# Conclusion

Our findings show that, in patients with HFrEF the NYHA classification overestimates the proportion of patients with FC I as compared with the CPET. The SAS provides

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reclassification of these patients, correct in most cases, with a better performance in detecting symptomatic patients with HF.

# **Author Contributions**

Conception and design of the research and Writing of the manuscript: Azevedo ER, Simões MV; Acquisition of data: Azevedo ER, Crescencio JC, DCP Cunha, Tanaka DM, Oliveira LFL; Analysis and interpretation of the data: Azevedo ER, Crescencio JC, DCP Cunha, Tanaka DM, Oliveira LFL, Simões MV; Statistical analysis: Azevedo ER, Schmidt A, Tanaka DM, Oliveira LFL, Simões MV; Critical revision of the manuscript for important intellectual content: Schmidt A, Simões MV.

#### Potential conflict of interest

No potential conflict of interest relevant to this article was reported.

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#### Study association

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#### Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo under the protocol number 4033/2017. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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