

Differential Associations of Maximal Handgrip Strength and Force-Time Curve Indicators with Functional Status in Heart Failure – A multicentre cross-sectional study from the NutriC project

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Abstract

Background

Maximal handgrip strength (mHGS) is a widely used marker of muscle function and has been associated with clinical outcomes in patients with heart failure. However, it only reflects peak force and does not capture the full dynamics of muscle contraction. This study investigated the association between mHGS and force-time curve indicators with cardiac functional status in patients with heart failure.

Methods

This cross-sectional multicentre study included 207 ambulatory patients (45.4% women; 72 ± 12.2 years) with heart failure from three Portuguese hospitals. mHGS was assessed using a wireless digital dynamometer, allowing derivation of force-time curve indicators (total, pre-, and post-peak area under the force-time curve (AUC)). Cardiac functional status was evaluated using the New York Heart Association (NYHA) classification. Multinomial logistic regression models were performed with NYHA functional class as the dependent variable, using class I as the reference category. Results are presented as odds ratios (OR) with 95% confidence intervals (CI).

Results

Overall, 30% of outpatients were classified as NYHA I, 52.2% as class II, and 17.9% as class III. In multivariable analysis, participants in the lowest quartile of right-hand mHGS had 6.83-fold higher odds of being classified as NYHA class III compared with those in the highest quartile (95% CI: 1.22–38.36). For right-hand total AUC, participants in the lowest quartile had 11.97-fold higher odds of being classified as NYHA class III (95% CI: 2.29–62.52). The association was stronger when the model was further adjusted for undernutrition risk: OR = 12.49 (95% CI: 2.29–68.26). Left-hand associations were not significant.

Conclusions

Total AUC showed stronger associations with cardiac functional status than mHGS, suggesting that force-time curve indicators may provide additional discrimination of functional impairment in heart failure.

Background

Heart failure is a complex clinical syndrome characterised by impaired cardiac function resulting from multiple cardiovascular aetiologies and accompanied by systemic neurohormonal activation, chronic low-grade inflammation, and increased oxidative stress⁽¹⁾. Reduced cardiac output leads to impaired

tissue perfusion and compromised blood flow in skeletal muscle. Consequently, individuals with heart failure develop a wide range of skeletal muscle abnormalities, including alterations in muscle fibre type composition, with a reduced proportion of type I fibres and an increased proportion of type II fibres, impaired contractile properties, mitochondrial dysfunction, and elevated circulating inflammatory cytokines(2). This pathophysiological cascade contributes not only to adverse myocardial remodelling but also to a progressive loss of peripheral muscle mass and strength(3). These peripheral muscular impairments are closely associated with reduced exercise tolerance, poor cardiorespiratory fitness, and increased physical inactivity(4–6), ultimately exacerbating symptom burden and disease severity, as reflected by a higher New York Heart Association (NYHA) functional class.

Maximal handgrip strength (mHGS) is a simple, non-invasive, and cost-effective measure of overall muscle strength and physical functional status. Growing evidence supports an independent association between mHGS and clinically relevant outcomes in heart failure, making this measure a leading assessment tool in this population. Pavasini *et al*(7) demonstrated that low mHGS predicts all-cause mortality, cardiac death, and hospital admission for heart failure in patients with cardiac disorders. Similarly, data from a recent meta-analysis by Wang *et al*(8) reveals that low mHGS values are associated with poorer clinical outcomes in individuals with heart failure. Moreover, a prospective cohort study(9) including 4654 participants from the UK Biobank showed that higher mHGS levels were associated with lower cardiac hypertrophy and less adverse cardiac remodelling, both of which are linked to reduced cardiovascular risk. Notwithstanding its clinical relevance, mHGS represents a static measure of peak force production and does not capture the dynamic characteristics of muscle contraction, which are particularly relevant in chronic conditions such as heart failure, where both central and peripheral impairments coexist(10).

In this context, the force-time curve derived from handgrip assessments may offer a more comprehensive evaluation of muscle function by characterising force production throughout the contraction period. Exploration of these dynamic force-time curve indicators may enhance the understanding of skeletal muscle dysfunction in heart failure, therefore improving the ability to discriminate functional impairment across NYHA classes.

Despite the recognised prognostic value of mHGS, evidence regarding its association with functional status, particularly NYHA classification, remains limited. To the best of our knowledge, the potential role of force-time curve indicators in this context has not yet been explored.

Therefore, this multicentre cross-sectional study, conducted within the framework of the NutriC project – *Nutrition and Functional Status in Heart Failure*, aimed to assess the association between force-time curve indicators and cardiac functional status in ambulatory patients with heart failure, and to determine whether these dynamic measures provide additional discrimination beyond maximal handgrip strength.

Methods

Study setting and sample

This multicentre cross-sectional study was conducted in heart failure outpatient clinics of three Portuguese tertiary hospitals between March 2023 and April 2024. Data were obtained within the framework of the NutriC project (Nutrition and Functional Status in Heart Failure), a branch of the NutriFunction project. Patients aged 18 years or older with a clinically validated diagnosis of heart failure, according to the European Society of Cardiology criteria(11), were recruited from medical appointment lists. Exclusion criteria included total disability of both upper limbs, pregnancy, lactation, and inability to provide oral and written informed consent.

Sociodemographic, lifestyle, nutritional and anthropometric measurements

Sociodemographic characteristics collected included sex, age, education level, marital status, occupation, and professional activity. Lifestyle variables comprised tobacco use and alcohol consumption. Physical activity was evaluated using the International Physical Activity Questionnaire – Short Form, validated for the Portuguese population(12), and categories were defined as inactive, minimally active, and active.

Risk of undernutrition was assessed using the Malnutrition Universal Screening Tool (MUST)(13) in participants aged < 65 years and the Mini Nutritional Assessment - Short Form (MNA®-SF)(14) in those aged ≥ 65 years.

Anthropometric measurements (body weight, height, hand length and breadth, mid arm, leg and waist circumferences, and triceps, calf and adductor pollicis thicknesses) were collected by trained, registered nutritionists in accordance with the International Society for the Advancement of Kinanthropometry (ISAK) protocol(15). Prior to data collection, the technical error of measurement was assessed for all anthropometric variables, and detailed procedures have been described previously(16).

Gait speed was calculated by dividing the distance travelled (4.6 m) on a flat, unobstructed path by the time (s) taken to cover that distance(17, 18).

Clinical data from outpatients with heart failure

Clinical data were collected during routine cardiology and internal medicine appointments and retrieved from medical records. Heart failure symptom severity was classified according to the New York Heart Association (NYHA) functional classification(19), which comprises four classes reflecting increasing symptom burden and limitation in physical activity. Class I indicates no limitation during ordinary physical activity; Class II describes patients who are comfortable at rest but develop symptoms during ordinary activity; Class III is characterised by marked limitation of physical activity, with symptoms occurring during less than ordinary activity despite comfort at rest; and Class IV includes patients with

symptoms at rest and an inability to perform any physical activity without discomfort. Patients classified as NYHA class IV were excluded due to limited ability to comply with the study protocol.

Gathered data also included heart failure aetiology, history of myocardial infarction, atrial fibrillation, diabetes mellitus, hypertension, dyslipidaemia, and medication use. Heart failure phenotypes were categorised as heart failure with reduced ejection fraction (HFrEF), mildly reduced ejection fraction (HFmrEF), or preserved ejection fraction (HFpEF) based on LVEF values of $\leq 40\%$, $41-49\%$, and $\geq 50\%$, respectively(11).

Handgrip strength assessment and force-time curve analysis

Handgrip strength was assessed using a wireless digital dynamometer (GripWise®, Wisify Tech Solutions, Porto, Portugal), which enables continuous acquisition of force signals and detailed analysis of force-time curves. The device operates at a sampling frequency of 100 Hz, with a resolution of 100 gf and a measurement range of ± 140 kgf. Data were transmitted via bluetooth to a dedicated mobile application (iOS or Android), allowing real-time visualisation of the force-time curve and automatic storage in a remote database. The validity of the prototype has previously been established by comparison with the Jamar Plus Hand dynamometer (Sammons Preston, Bolingbrook, IL)(20).

All measurements were performed according to the standardised protocol recommended by the American Society of Hand Therapists(21). Participants received standardised instructions to perform a maximal voluntary grip contraction, and strong verbal encouragement was provided throughout each attempt. Three trials were performed for each hand, starting with the dominant hand, with continuous force data recorded. mHGS and force-time curve indicators were calculated as the mean of the three trials. Each acquisition lasted 15 seconds, in accordance with the device validation protocol. Maximal handgrip strength values were expressed in kilogram-force (kgf). Each 15-second trial yields 1500 force measurements, and with three trials per hand, a total of 9000 measurements were collected per participant, enabling detailed construction of the handgrip force-time curve and extraction of dynamic handgrip parameters beyond maximal force:

- Total area under the force-time curve (total AUC, kgf-s), defined as the integral of force over time during the entire contraction and calculated using the trapezoidal rule:

$$A = \frac{(F_1 + F_2)}{2} \times (t_2 - t_1)$$

where F_1 and F_2 were the force values at two consecutive points, and t_1 and t_2 were the times corresponding to those points. The total area under the force-time curve was then obtained by summing the areas of all trapezoids:

$$A_{total} = \sum_{i=1}^{n-1} \frac{(F_i + F_{i+1})}{2} \times (t_{i+1} - t_i)$$

where n is the total number of data points.

- Pre-peak area under the force-time curve (pre-peak AUC, kgf-s), defined as the integral of force from contraction onset to peak force:

$$A_{pre-peak} = \sum_{i=1}^{p-1} \frac{(F_i + F_{i+1})}{2} \times (t_{i+1} - t_i)$$

where p represents the index corresponding to the time point at which peak force is attained.

- The post-peak area under the force-time curve (post-peak AUC, kgf-s), defined as the difference between total AUC and pre-peak AUC:

$$A_{post-peak} = A_{total} - A_{pre-peak}$$

Statistical analysis

Participant characteristics were described according to NYHA functional class. Normality of continuous variables was assessed using skewness and kurtosis, as well as visual inspection of histograms. Continuous variables were presented as mean (μ) and standard deviation (SD) or median (Md) and interquartile range (IQR), as appropriate. Categorical variables are presented as absolute frequencies (n) and percentages (%).

Between-group comparisons were performed using one-way ANOVA with Tukey post-hoc tests for normally distributed variables, and the Kruskal-Wallis test with pairwise comparisons using Mann-Whitney U tests with Bonferroni correction for non-normally distributed variables. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate, with post-hoc analyses based on adjusted standardised residuals.

Sex-specific quartiles of mHGS and handgrip strength force-time curve indicators were created. Associations between these variables and NYHA functional class were examined using multinomial logistic regressions, with NYHA class I and the highest quartile (quartile 4) as reference categories. Odds ratios (OR) and 95% confidence intervals (95% CI) were reported. Separate models were constructed for mHGS and for each force-time curve indicator. All models were adjusted for sex, age, recruitment centre, LVEF categories, height, adductor pollicis thickness, and hand breadth (Model 1), and additionally adjusted for risk of undernutrition (Model 2). Tests for linear trend across quartiles were performed by modelling quartiles as an ordinal variable.

Collinearity was assessed using variance inflation factors (VIF), with all values < 2 indicating no relevant multicollinearity(22). Sensitivity analyses included (i) exclusion of eight left-handed participants, and (ii) additional adjustment for physical activity level. All statistical tests were two-tailed, and a significance level of $p < 0.05$ was adopted. Analyses were performed using IBM SPSS Statistics version 30.0 (IBM Corp., Armonk, NY, USA).

Ethics

The NutrIC project received ethical approval from the Ethics Committee of the Faculty of Nutrition and Food Sciences of the University of Porto (reference 115/2022). Additional approvals were obtained from the Board of Directors of Centro Hospitalar de Entre Douro e Vouga (reference 12-01-2023), the Ethics Committee for Health and the Scientific and Research Commission of the Serviço de Saúde da Região Autónoma da Madeira (reference 23/2023), and the Ethics Committee and institutional review boards of Centro Hospitalar Universitário de Santo António (reference 2023.117).

The study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants before enrolment, detailing the study procedures and authorising the dissemination of results. Participant confidentiality and anonymity were strictly maintained throughout the research process.

Results

The NutrIC project included 207 outpatients (45.4% women), aged 34–95 years, with a mean age of 72 ± 12.2 years. The sociodemographic, clinical, anthropometric, functional, and nutritional characteristics of the participants according to the three NYHA functional classes are presented in Table 1.

Outpatients in higher NYHA classes were older, with post hoc analyses indicating that patients in NYHA classes II and III were older than those in class I. They were also more frequently inactive in terms of professional status, with NYHA I patients more often active and NYHA II patients more often inactive. A higher frequency of undernutrition risk was observed in NYHA class III (56.8%), with a post-hoc analysis indicating a lower-than-expected risk in NYHA I and a higher-than-expected risk in NYHA III.

Additionally, gait speed was lower in higher NYHA classes, with NYHA I patients presenting higher values compared to those in NYHA II and III. Waist circumference differed across NYHA classes, with higher values observed in patients in more advanced classes; however, post hoc comparisons between individual classes revealed non-significant results.

Regarding clinical characteristics, no differences were observed across NYHA classes for LVEF, heart failure phenotype, or most comorbidities.

Table 1

Summary of participants' sociodemographic, anthropometric, functional, nutritional and clinical characteristics in a sample of outpatients with heart failure according to NYHA classification (n = 207).

Sex, n (%)	NYHA I (n = 62, 30%)	NYHA II (n = 108, 52.2%)	NYHA III (n = 37, 17.9%)	p-value
				0.321
Female	24 (38.7)	50 (46.3)	20 (54.1)	
Male	38 (61.3)	58 (53.7)	17 (45.9)	
Centres of data collection, n (%)				0.065
Centre 1 (ULS-EDV)	20 (32.3)	36 (33.3)	20 (54.1)	
Centre 2 (SESARAM)	22 (35.5)	27 (25.0)	9 (24.3)	
Centre 3 (ULS-SA)	20 (32.3)	45 (41.7)	8 (21.6)	
Age (years), μ (SD)	68.4 (12.6)	73.1 (10.7)	75.0 (14.2)	0.014
School years, Md (IQR)	4 (2)	4 (2)	4 (1)	0.399
Marital status, n (%)				0.598
Married or common law union	27 (43.5)	51 (47.2)	20 (54.1)	
Single, divorced or widowed	35 (56.5)	57 (52.8)	17 (45.9)	
Professional status, n (%)				0.001
Inactive	48 (77.4)	102 (94.4)	35 (94.6)	
Active	14 (22.6)	6 (5.6)	2 (5.4)	
Physical activity, n (%)				0.054
Inactive or minimally active	50 (82.0)	100 (92.6)	34 (94.4)	
Active	11 (18.0)	8 (7.4)	2 (5.6)	
Smoking habits, n (%)				0.660
Non-smoker	33 (53.2)	51 (47.2)	20 (54.1)	
Former or current smoker	29 (46.8)	57 (52.8)	17 (45.9)	
Drinking habits, n (%)				0.750
No current alcohol consumption	33 (53.2)	51 (47.2)	18 (48.6)	
Current alcohol consumption	29 (46.8)	57 (52.8)	19 (51.4)	

Sex, n (%)	NYHA I (n = 62, 30%)	NYHA II (n = 108, 52.2%)	NYHA III (n = 37, 17.9%)	p-value
				0.321
Heart failure aetiology, n (%)				0.514
Dilated cardiomyopathy	17 (27.4)	31 (28.7)	12 (32.4)	
Ischemic	16 (25.8)	26 (24.1)	6 (16.2)	
Valve disease	7 (11.3)	16 (14.8)	3 (8.1)	
Myocarditis	2 (3.20)	0 (0)	1 (2.9)	
Hypertrophic	0 (0)	0 (0)	1 (2.7)	
Others	9 (14.5)	22 (20.4)	6 (16.2)	
Unknown etiology	8 (12.9)	10 (9.3)	5 (13.5)	
LVEF categories, n (%)				0.218
HFpEF	23 (37.1)	39 (36.1)	17 (45.9)	
HFmrEF	18 (29.0)	19 (17.6)	5 (13.5)	
HFrEF	21 (33.9)	50 (46.3)	15 (40.5)	
Medicines, n (%)				
ACE inhibitors and ARBs	20 (32.3)	36 (33.3)	14 (37.8)	0.841
Beta blockers	51 (82.3)	85 (78.7)	31 (83.8)	0.741
Aldosterone antagonists	37 (59.7)	61 (56.5)	15 (40.5)	0.310
Sacubitril/Valsartan	30 (48.4)	44 (40.7)	14 (37.8)	0.697
Loop diuretics	38 (61.3)	80 (74.1)	33 (89.2)	0.034
Oral anticoagulants	33 (53.2)	61 (56.5)	27 (73.0)	0.130
Acetylsalicylic acid	18 (29.0)	28 (25.9)	7 (18.9)	0.701
Nitrates	3 (4.8)	12 (11.1)	1 (2.7)	0.312
Digoxin	5 (8.1)	8 (7.4)	2 (5.4)	0.882
Antiarrhythmics	8 (12.9)	15 (13.9)	2 (5.4)	0.382
Antidiabetics	49 (79.0)	87 (80.6)	25 (67.6)	0.405
SGLT2 inhibitors	46 (74.2)	84 (79.2)	25 (69.4)	0.456

Sex, n (%)	NYHA I (n = 62, 30%)	NYHA II (n = 108, 52.2%)	NYHA III (n = 37, 17.9%)	p-value
				0.321
Statins	49 (79.0)	76 (70.4)	21 (56.8)	0.063
Antidepressants	18 (29.0)	39 (36.1)	12 (32.4)	0.752
Anxiolytics	13 (21.0)	22 (20.4)	9 (24.3)	0.884
History of stroke, n (%)	12 (19.4)	18 (16.7)	7 (18.9)	0.985
Atrial fibrillation, n (%)	29 (46.8)	56 (51.9)	20 (54.1)	0.549
Diabetes, n (%)	27 (43.5)	55 (50.9)	15 (40.5)	0.359
Dyslipidemia, n (%)	43 (69.4)	79 (73.1)	24 (64.9)	0.611
Hypertension, n (%)	49 (79.0)	93 (86.1)	30 (81.1)	0.219
Weight, kg, μ (SD)	73.6 (13.0)	76.3 (16.2)	75.8 (19.1)	0.541
Height, cm, μ (SD)	161.5 (9.4)	160.9 (9.1)	159.3 (9.8)	0.517
Hand length, μ (SD)	18.50 (1.02)	18.29 (1.19)	17.96 (1.22)	0.076
Hand breadth, μ (SD)	8.15 (0.64)	8.11 (0.61)	7.98 (0.60)	0.413
Adductor pollicis thickness, mm, μ (SD)	15.76 (4.12)	15.46 (3.88)	14.45 (4.04)	0.297
BMI classification, n (%)				0.674
Underweight	1 (1.6)	1 (0.9)	0 (0.0)	
Normal	14 (22.6)	20 (18.5)	9 (24.3)	
Overweight	28 (45.2)	42 (38.9)	12 (32.4)	
Obese	19 (30.6)	45 (41.7)	16 (43.2)	
Mid arm circumference, cm, μ (SD)	28.9 (4.0)	29.8 (4.8)	28.6 (5.3)	0.293
Tricipital skinfold thickness, mm, μ (SD)	15.5 (6.4)	17.6 (8.9)	15.7 (7.9)	0.214
Mid arm muscle circumference, cm, μ (SD)	24.0 (3.6)	24.3 (3.3)	23.3 (3.4)	0.347
Leg circumference, cm, μ (SD)	36.1 (4.0)	36.9 (4.3)	37.3 (5.6)	0.424
Calf skinfold thickness, mm, μ (SD)	14.7 (8.6)	15.9 (8.9)	16.4 (9.0)	0.602

Sex, n (%)	NYHA I (n = 62, 30%)	NYHA II (n = 108, 52.2%)	NYHA III (n = 37, 17.9%)	p-value
				0.321
Leg muscle circumference, cm, Md (IQR)	31.5 (5.4)	31.8 (5.0)	30.9 (6.3)	0.666
Waist circumference, cm, Md (IQR)	98.0 (12.9)	101.4 (14.9)	103.6 (21.0)	0.034
Composite risk of undernutrition				0.007
No risk of undernutrition	46 (74.2)	71 (65.7)	16 (43.2)	
Medium/high risk of undernutrition	16 (25.8)	37 (34.3)	21 (56.8)	
Gait speed, m/s, μ (SD)	0.95 (0.27)	0.81 (0.29)	0.69 (0.30)	< 0.001

ULS-EDV: Unidade Local de Saúde de Entre Douro e Vouga; SESARAM: Serviço de Saúde da Região Autónoma da Madeira; ULS-SA: Unidade Local de Saúde de Santo António; NYHA: New York Heart Association; HFpEF: Heart Failure with preserved Ejection Fraction; HFmrEF: Heart Failure with mildly reduced Ejection Fraction; HFrEF: Heart Failure with reduced Ejection Fraction; ACE: angiotensin-converting enzyme; ARBs: angiotensin receptor blockers; SGLT2: sodium-glucose cotransporter 2. Continuous variables are presented as mean (μ) and standard deviation (SD) or median (Md) and interquartile range (IQR), as appropriate. Normally distributed variables were compared using one-way ANOVA with Tukey post-hoc tests, whereas non-normally distributed variables were analysed using the Kruskal-Wallis test. Categorical variables were compared using the chi-square (χ^2) test or Fisher's exact test, as appropriate. Data may not sum to the total sample size due to missing values. Bold text indicates a statistically significant difference with a *p*-value less than 0.05.

Mean mHGS and force-time curve indicators according to NYHA functional class are presented in Table 2. Significant differences across NYHA classes were observed for mHGS (right and left), total AUC (right and left), and post-peak AUC (right and left). Post-hoc analyses indicated that patients in NYHA class I had higher values compared to those in NYHA classes II and III, whereas no differences were observed between classes II and III after Bonferroni correction.

For the pre-peak AUC, an overall difference was observed for the right hand; however, pairwise comparisons between NYHA classes were not significant after Bonferroni correction. No differences were observed for the left hand.

Table 2

Maximal handgrip strength and force-time curve indicators according to NYHA classification in a sample of outpatients with heart failure (n = 207).

Maximal handgrip strength, kgf, Md (IQR)	NYHA I (n = 62, 30%)	NYHA II (n = 108, 52.2%)	NYHA III (n = 37, 17.9%)	p- value
Right	22.1 (14.5)	17.3 (11.6)	14.2 (8.8)	0.001
Left	19.6 (12.6)	15.0 (9.2)	13.2 (7.9)	0.016
Total area under the force-time curve, kgf-s, Md (IQR)				
Right	256.8 (131.2)	199.0 (142.6)	155.5 (145.5)	< 0.001
Left	219.4 (126.3)	177.6 (118.6)	141.4 (98.1)	0.002
Pre-peak area under the force-time curve, kgf-s, Md (IQR)				
Right	53.3 (59.4)	38.2 (38.1)	35.5 (30.2)	0.044
Left	30.8 (39.4)	27.8 (34.9)	24.0 (21.6)	0.154
Post-peak area under the force- time curve, kgf-s, Md (IQR)				
Right	210.4 (138.3)	152.1 (120.3)	121.8 (96.5)	0.001
Left	180.2 (128.5)	137.5 (92.0)	114.4 (95.2)	0.005

Given the distribution of the data and the sample size across NYHA subgroups, all continuous variables are presented as median (Md) and interquartile range (IQR) and were compared using the Kruskal-Wallis test. Bold text indicates a statistically significant difference with a *p*-value less than 0.05.

The multinomial logistic regression analysis examining the associations between sex-specific quartiles of mHGS and force-time curve indicators with NYHA functional class is presented in Table 3. For mHGS, individuals in the lowest quartile of right-hand strength had higher odds of being classified as NYHA class III compared with those in the highest quartile (Model 1: OR = 6.83; 95% CI: 1.22–38.36). After additional adjustment for undernutrition risk, this association became non-significant (Model 2: OR = 5.62; 95% CI: 0.95–33.26).

Stronger associations were observed for total area under the force-time curve. Specifically, participants in the lowest quartile of right-hand total AUC had higher odds of being classified as NYHA class III vs. NYHA class I compared with those in the highest quartile (Model 1: OR = 11.97; 95% CI: 2.29–62.52), increasing to 12.49 after further adjustment for risk of undernutrition (Model 2: OR = 12.49; 95% CI: 2.29–68.26). Overall, pre-peak AUC showed a heterogeneous pattern, with no significant linear trend across quartiles. Finally, no associations were observed for post-peak AUC. When the models were further adjusted for physical activity level, the results remained robust for right-hand mHGS (NYHA III vs. NYHA I: OR = 6.40; 95% CI: 1.13–36.42) and for right-hand total AUC (NYHA III vs. NYHA I: OR = 11.28; 95% CI: 2.13–59.64).

Table 3

Multinomial logistic regression analyses of maximal handgrip strength and force-time curve indicators (quartiles) in relation to NYHA functional class in outpatients with heart failure (n = 207).

	Model 1		Model 2	
	NYHA II vs I	NYHA III vs I	NYHA II vs I	NYHA III vs I
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Maximal handgrip strength				
Right				
Quartile 1	2.89 (0.87–9.66)	6.83 (1.22–38.36)	2.77 (0.83–9.27)	5.62 (0.95–33.26)
Quartile 2	1.36 (0.43–4.37)	8.10 (1.49–44.18)	1.27 (0.39–4.12)	6.76 (1.19–38.39)
Quartile 3	1.39 (0.54–3.61)	2.95 (0.65–13.44)	1.36 (0.52–3.52)	2.66 (0.56–12.51)
Quartile 4	(ref.)	(ref.)	(ref.)	(ref.)
P for trend	0.080	0.035	0.094	0.071
Left				
Quartile 1	1.85 (0.60–5.67)	1.84 (0.44–7.81)	1.83 (0.60–5.62)	1.63 (0.37–7.12)
Quartile 2	3.57 (1.11–11.57)	2.51 (0.55–11.42)	3.50 (1.07–11.49)	2.04 (0.44–9.52)
Quartile 3	1.33 (0.51–3.48)	0.77 (0.19–3.15)	1.34 (0.51–3.53)	0.85 (0.20–3.54)
Quartile 4	(ref.)	(ref.)	(ref.)	(ref.)
P for trend	0.185	0.210	0.213	0.351
Total area under the force-time curve				
Right				
Quartile 1	3.30 (0.94–11.53)	11.97 (2.29–62.52)	3.32 (0.95–11.59)	12.49 (2.29–68.26)
Quartile 2	1.78 (0.62–5.11)	3.39 (0.75–15.45)	1.74 (0.60–5.00)	3.48 (0.74–16.29)
Quartile 3	1.56 (0.61–4.01)	1.80 (0.40–8.11)	1.63 (0.63–4.21)	2.24 (0.48–10.55)
Quartile 4	(ref.)	(ref.)	(ref.)	(ref.)

	Model 1		Model 2	
	NYHA II vs I	NYHA III vs I	NYHA II vs I	NYHA III vs I
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
<i>P</i> for trend	0.076	0.002	0.078	0.002
Left				
Quartile 1	2.81 (0.81–9.70)	4.58 (0.90–23.34)	2.74 (0.80–9.40)	4.47 (0.83–24.13)
Quartile 2	2.27 (0.70–7.42)	1.77 (0.33–9.61)	2.23 (0.68–7.30)	1.74 (0.31–9.85)
Quartile 3	1.13 (0.43–2.99)	1.02 (0.23–4.50)	1.71 (0.44–3.10)	1.43 (0.30–6.78)
Quartile 4	(ref.)	(ref.)	(ref.)	(ref.)
<i>P</i> for trend	0.067	0.030	0.079	0.059
Pre-peak area under the force-time curve				
Right				
Quartile 1	1.62 (0.63–4.17)	2.21 (0.59–8.33)	1.58 (0.61–4.10)	2.04 (0.53–7.86)
Quartile 2	2.17 (0.82–5.78)	4.59 (1.24–16.98)	2.10 (0.79–5.60)	4.67 (1.23–17.61)
Quartile 3	3.19 (1.22–8.31)	2.10 (0.52–8.50)	3.28 (1.25–8.63)	2.33 (0.55–9.77)
Quartile 4	(ref.)	(ref.)	(ref.)	(ref.)
<i>P</i> for trend	0.381	0.101	0.414	0.147
Left				
Quartile 1	1.71 (0.58–5.01)	3.06 (0.72–13.08)	1.64 (0.55–4.89)	2.28 (0.51–10.18)
Quartile 2	0.32 (0.12–0.85)	1.57 (0.40–6.18)	0.32 (0.12–0.84)	1.58 (0.39–6.42)
Quartile 3	2.08 (0.73–5.93)	2.34 (0.53–10.37)	2.04 (0.71–5.85)	2.10 (0.46–9.64)
Quartile 4	(ref.)	(ref.)	(ref.)	(ref.)
<i>P</i> for trend	0.692	0.290	0.599	0.524
Post-peak area under the force-time curve				

	Model 1		Model 2	
	NYHA II vs I	NYHA III vs I	NYHA II vs I	NYHA III vs I
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Right				
Quartile 1	1.60 (0.52–4.92)	4.22 (0.92–19.45)	1.60 (0.52–4.93)	4.26 (0.89–20.38)
Quartile 2	1.30 (0.45–3.74)	2.06 (0.44–9.65)	1.30 (0.45–3.74)	2.07 (0.43–10.03)
Quartile 3	1.38 (0.53–3.61)	2.00 (0.47–8.43)	1.42 (0.54–3.73)	2.29 (0.53–9.90)
Quartile 4	(ref.)	(ref.)	(ref.)	(ref.)
<i>P</i> for trend	0.464	0.066	0.466	0.082
Left				
Quartile 1	1.97 (0.63–6.15)	3.12 (0.66–14.70)	2.02 (0.65–6.28)	3.30 (0.66–16.38)
Quartile 2	2.65 (0.82–8.57)	2.27 (0.44–11.77)	2.61 (0.82–8.38)	2.14 (0.39–11.59)
Quartile 3	1.08 (0.40–2.91)	1.01 (0.22–4.59)	1.17 (0.42–3.21)	1.48 (0.30–7.27)
Quartile 4	(ref.)	(ref.)	(ref.)	(ref.)
<i>P</i> for trend	0.117	0.064	0.118	0.105

Model 1: adjusted for sex, age, centres of data collection, left ventricular ejection fraction categories, height, hand breadth, and adductor pollicis thickness; Model 2: additionally adjusted for risk of undernutrition. NYHA class I was used as the reference category. Results are presented as odds ratios (OR) with 95% confidence intervals (CI). Bold text indicates a statistically significant difference with a *p*-value less than 0.05.

Sensitivity analysis showed that excluding left-handed participants (*n* = 8) led to minimal changes in the ORs for the main outcomes. For total AUC, the OR estimates for NYHA class III vs. NYHA class I changed from 11.97 (95% CI: 2.29–62.52) to 11.62 (95% CI: 2.12–63.55), corresponding to a -3.0% change. For mHGS, the OR for NYHA class III vs. NYHA class I decreased from 6.83 (95% CI: 1.22–38.36) to 6.01 (95% CI: 1.01–35.77), representing a 12.0% decrease. Finally, for total AUC and after additional adjustment for undernutrition risk, the OR for NYHA class III vs. NYHA class I changed from 12.49 (95% CI: 2.29–68.26) to 12.80 (95% CI: 2.23–73.51), corresponding to a + 2.5% change.

Discussion

In this multicentre cross-sectional study of ambulatory patients with heart failure, both mHGS and force-time curve indicators were inversely associated with NYHA functional class. Notably, right-hand total AUC demonstrated stronger and more consistent associations with functional status than mHGS. In models adjusted for sex, age, recruitment centre, LVEF categories, and anthropometric variables, individuals in the lowest quartile of right-hand total AUC had 11.97-fold higher odds of being classified as NYHA class III compared to those in the highest quartile, whereas for mHGS the corresponding increase was 6.83-fold. When additionally adjusting for undernutrition risk, the association for right-hand total AUC remained robust, with individuals in the lowest quartile presenting 12.49-fold higher odds of being classified as NYHA class III. In contrast, the association between mHGS and NYHA functional class was no longer significant after this adjustment. These findings suggest that total AUC, which captures the overall force produced throughout the contraction period, may provide additional information on functional impairment beyond peak force alone.

These findings are partially consistent with previous research highlighting the prognostic value of mHGS in heart failure. However, there is currently a lack of evidence evaluating force-time curve indicators, such as total AUC, precluding direct comparison with our findings. A cross-sectional study conducted by Duarte *et al*(23) including 500 patients with congestive heart failure, showed that each 1 kgf increase in mHGS was associated with a 2% reduction in the odds of more severe heart failure according to the NYHA classification, even after controlling for LVEF. A meta-analysis by Pavasini *et al*(7) demonstrated that low mHGS predicts all-cause death, cardiac death, and hospitalisation in this population. Results from the Prospective Urban-Rural Epidemiology (PURE) study(24), a large longitudinal population study with over 142,000 participants across 17 countries, showed that each 5 kgf decrease in mHGS was associated with increased risks of heart attack and stroke, and also that mHGS was a stronger predictor of all-cause and cardiovascular mortality than systolic blood pressure. Similarly, a 2023 meta-analysis(8) of 15 cohort studies revealed that each 1 kgf decrease in mHGS increased the mortality risk in patients with heart failure by approximately 8%. Additionally, they also found that patients with low mHGS had a higher incidence of heart failure rehospitalisation, independently of age, country, and heart failure type. Taken together, these findings reinforce the association between reduced mHGS and adverse clinical outcomes in heart failure.

Our findings extend this evidence by exploring the dynamic characteristics of muscle function through force-time curve indicators. From a physiological perspective, total AUC may reflect both the capacity to generate force and the ability to sustain it over time. This integrated measure may be particularly relevant in heart failure, where skeletal muscle dysfunction, early fatigue, impaired oxidative metabolism, and reduced physical activity frequently coexist. Unlike mHGS, which captures only the highest instantaneous force, total AUC may better represent the overall contraction profile and therefore be more closely aligned with perceived functional limitation.

In contrast, pre-peak AUC showed no consistent association with functional status. Although isolated associations were observed in specific quartiles, these did not show a consistent pattern and were not supported by a significant linear trend (Table 3). These heterogeneous findings may reflect the fact that

pre-peak AUC is particularly sensitive to technical and behavioural variability during test execution, such as delayed muscle activation, participant hesitation, and differences in reaction time. As this indicator depends on the immediate response to the initiation signal, even small variations in reaction time may substantially influence the recorded force profile.

Post-peak AUC was not associated with NYHA class in this sample. Although some non-significant trends were observed in the right hand (particularly for NYHA class III), these did not reach statistical significance or show a consistent pattern across quartiles. This may suggest that force decay following peak contraction is less strongly related to overall functional status in heart failure. Additionally, this phase of the contraction may be more susceptible to variability, including factors such as participant motivation, fatigue, and reduced control during force release, which could attenuate potential associations.

Taken together, these findings suggest that isolated phases of the force-time curve do not meaningfully discriminate functional status in heart failure. In contrast, the overall contraction profile, total AUC, may better capture clinically relevant differences in muscle function.

The observed associations were identified for the right hand, but not for the left. This pattern remained unchanged after excluding participants with left-hand dominance, suggesting that it is unlikely to be explained solely by handedness. A possible explanation is that the right hand may provide a more consistent or sensitive measure of muscle function, potentially due to habitual use in daily activities and more efficient motor unit recruitment. In contrast, the left hand may be more susceptible to variability, which could reduce its ability to detect associations with cardiac functional status. Moreover, these associations remained consistent for total AUC after additional adjustment for undernutrition risk, and sensitivity analyses further adjusting for physical activity level yielded similar results. These findings suggest that differences in nutritional status or habitual physical activity do not solely explain the associations. Considering that the NYHA classification is largely based on patient-reported symptoms and functional limitations during daily activities, the persistence of these associations reinforces the potential of force-time curve indicators as objective markers of functional impairment.

Waist circumference was not included in the adjusted regression models. In patients with heart failure, this anthropometric measure may be influenced by fluid retention, abdominal distension, or ascites, particularly in more advanced stages of the syndrome. Consequently, waist circumference may not accurately reflect adiposity in this population and could introduce bias in the interpretation of associations with functional status.

This study presents several strengths. Firstly, to the best of our knowledge, this work is among the first to investigate dynamic handgrip strength indicators derived from the force-time curve in relation to heart failure severity. While mHGS is widely used as a marker of muscle function in clinical settings, few studies⁽²³⁾ have explored its association with NYHA functional classification, and the limited available evidence generally supports an inverse association. Importantly, no studies have directly compared the widely used and well-established measure, mHGS, with force-time curve indicators in relation to

functional status in patients with heart failure. Furthermore, although force-time curve indicators have been investigated in other populations and clinical conditions(25), their potential relevance for assessing the association between physical function and disease severity in heart failure has not been explored previously. By incorporating both conventional and dynamic indicators of muscle function, this study provides novel insights into the potential value of force-time curve analysis for a more detailed characterisation of functional impairment in outpatients with heart failure. Secondly, the present study benefited from the use of an innovative wireless digital dynamometer capable of high-frequency sampling, enabling continuous acquisition of force signals and a more detailed evaluation of muscle contraction dynamics beyond peak force. This device has been previously compared with the Jamar Plus Hand dynamometer, showing good agreement in handgrip strength measurements, which supports the comparability and reliability of the measurements obtained(20). Thirdly, the inclusion of participants from three different healthcare settings, including both mainland and insular hospitals, represents an additional strength of the study. This multicentre design introduced heterogeneity in clinical characteristics and healthcare contexts, which may enhance the external validity and broader relevance of the findings. Finally, the application of a standardised assessment protocol, combined with prior training of all investigators involved in data collection(16) and the previous evaluation of inter- and intra-observer reliability, supports the internal validity and consistency of the study measurements, including the force-time curve indicators.

Some limitations should also be acknowledged. First, the study sample consisted of a convenience sample of ambulatory patients with heart failure, which mainly represents clinically stable outpatients. Therefore, the results may not be fully generalisable to hospitalised patients or individuals with more advanced or unstable disease. In addition, patients classified as NYHA class IV were excluded from the study, as they were not able to perform the assessment protocol. Consequently, the present findings cannot be generalised to individuals with the most severe cardiac functional impairment. Second, the cross-sectional design limits the ability to infer causal relationships between mHGS, force-time curve indicators and heart failure functional status, and does not allow evaluation of their predictive value over time. Future longitudinal studies are warranted to assess whether these indicators can predict changes in clinical outcomes of outpatients with heart failure. Third, heart failure severity in this study was assessed primarily using NYHA functional classification and LVEF. While these measures are widely used in clinical practice, they may not fully capture all dimensions of heart failure severity. Other biomarkers, such as brain natriuretic peptide, could provide more sensitive or objective measures of cardiac dysfunction. However, these tests were not included in the patient's assessment routine. Finally, although handgrip assessment relies on maximal voluntary effort, which may introduce variability because performance can be influenced by participant motivation or understanding of the task, this potential source of variability was minimised through the use of a standardised assessment protocol, prior investigator training, and consistent verbal encouragement during testing.

Conclusion

In conclusion, this exploratory multicentre study suggests that total AUC, a dynamic handgrip force-time curve indicator, is more strongly associated with NYHA functional class than mHGS in ambulatory patients with heart failure. These findings indicate that profile-based measures of handgrip performance may provide additional insight into functional impairment beyond peak force alone. Longitudinal studies are needed to determine whether these indicators predict clinical outcomes and responsiveness to therapeutic interventions.

Abbreviations

NYHA

New York Heart Association

BMI

Body mass index

LVEF

Left-ventricular ejection fraction

HFrEF

Heart failure with reduced ejection fraction

HFmrEF

Heart failure with mildly reduced ejection fraction

HFpEF

Heart failure with preserved ejection fraction

mHGS

Maximal handgrip strength

Total AUC

Total area under the force-time curve

Pre-peak AUC

Pre-peak area under the force-time curve

Post-peak AUC

Post-peak area under the force-time curve

ULS-EDV

Unidade Local de Saúde de Entre Douro e Vouga

SESARAM

Serviço de Saúde da Região Autónoma da Madeira

ULS-SA

Unidade Local de Saúde de Santo António

MUST

Malnutrition Universal Screening Tool

MNA®-SF

Mini Nutritional Assessment - Short Form

ACE

angiotensin-converting enzyme
ARBs
angiotensin receptor blockers
SGLT2
sodium-glucose cotransporter 2.

Declarations

Ethics approval and consent to participate

The NutrIC project was approved by the Ethics Committee of the Faculty of Nutrition and Food Sciences of the University of Porto (reference 115/2022), the Board of Directors of Centro Hospitalar de Entre Douro e Vouga (12-01-2023), the Ethics Committee for Health and Scientific Commission of the Serviço de Saúde da Região Autónoma da Madeira (23/2023), and the Ethics Committee of Centro Hospitalar Universitário de Santo António (2023.117). The study was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent, and confidentiality and anonymity were strictly ensured.

Consent for publication

Not applicable.

Competing interests

The authors report no conflict of interest.

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Author Contribution

T.A., N.B., R.S.G., and R.V. contributed to the creation and design of the study; T.A and R.S.G were responsible for supervision; M.C.R., I.M., A.T., and R.B. participated in data collection; M.C.R., T.A., R.S.G., and R.V. performed the analysis; M.C.R. conducted the literature search, inserted the collected data, prepared the figures, and wrote the original manuscript. All authors critically reviewed this and previous versions of the paper.

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Data Availability

The datasets generated and analysed during this study are not publicly available due to ongoing research using the same data. However, they are available from the corresponding author upon reasonable request.

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