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The relationship between physical activity and appetite in patients with heart failure – a prospective observational study

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Introduction: Physical activity and appetite are important components for maintaining health. Yet, the association between physical activity and appetite in heart failure (HF) populations is not completely understood. The aim of the present study was to investigate the relationship between physical activity, functional capacity, and appetite in patients with HF.

Methods: Prospective observational study. In total, 186 patients diagnosed with heart failure, NYHA class II-IV (mean age 70.7, 30% female), were included. Physical activity was measured a multi-sensor actigraph for seven days and with a self-reported numeric rating scale. Physical capacity was measured by the six minute walk test. Appetite was measured using the Council on Nutrition Appetite Questionnaire. Data were collected at inclusion and after 18 months. A series of linear regression analyses, adjusted for age, NYHA class, and BNP were conducted.

Results: At baseline, higher levels of physical activity and functional capacity were significantly associated with a higher level of appetite in the unadjusted models. In the adjusted models, number of steps ($p=0.019$) and the six minute walk test ($p=0.007$) remained significant. At the 18-month follow-up, all physical activity variables and functional capacity were significantly associated with appetite in the unadjusted regression models. In the adjusted models, number of steps ($p=0.001$) and METs daily average ($p=0.040$) remained significant.

Conclusion: Higher level of physical activity measured by number of steps/day was associated with better self-reported appetite, both at baseline and the 18-month follow-up. Further research is needed to establish causality and explore the intertwined relationship between activity and appetite in patients with heart failure.

Keywords: Appetite, Heart Failure, Physical activity

Introduction

Appetite, defined as the “desire to eat” (1), is commonly decreased in patients with heart failure (HF). Many patients with HF have been found to have decreased appetite to a degree where they become at risk of malnutrition (2). This may lead to a decline in functional capacity (3, 4), impaired quality of life (5, 6), and poor survival (7, 8). Although decreased appetite can lead to a worse health outcome in patients with HF, the knowledge of factors associated with decreased appetite has primarily been described through metabolic processes (i.e., increased inflammation, neurohormonal activation), and disease severity (i.e., fluid accumulation in the gastrointestinal tract) (9, 10).

Physical activity is an important component of HF management (11). Physical activity, defined as any type of bodily movement to increase energy expenditure, includes leisure time physical activities, playing, active transportation, occupational and household activities. Increased physical activity has been associated with improved functional capacity, reduced morbidity, and enhanced quality of life (12). However, physical activity is a challenge for patients with HF, with recent studies describing that only 30%-56% are physically active at the recommended level (13, 14).

The relationship between physical activity and appetite has been studied in biological research. Physical activity increases the body’s energy consumption. To compensate for a negative energy balance, physical activity simultaneously increases appetite hormones (15). The relationship between physical activity and appetite are thought to be affected by both physiological and hormonal mechanisms, as well as the body’s overall resting metabolic rate (15).

Physical activity and appetite are important components for maintaining physical health. Despite the pivotal role that physical activity plays in HF management, the relationship

between physical activity and appetite is not well understood. To our knowledge, there are no previous studies examining the association between physical activity and appetite in patients with HF. Studies examining associations between physical activity and appetite have mainly been performed in obese populations and from a physiological perspective (16-18). A few studies have investigated the associations between physical activity and appetite from a psychosocial perspective. A cross-sectional study of frail elderly people showed a significant association between walking speed and appetite and that poor appetite predicts physical disability over time (3). In contrast, no such associations between physical activity and appetite were found in a study including elderly individuals (19).

The authors of the present study previously found that functional capacity measured by the six minute walk test was associated with decreased appetite (20). In the present study, the goal was to investigate this relationship further, including both objective and subjective measures of physical activity. The aim of the study was therefore to investigate the relationship between physical activity, functional capacity and appetite in patients with HF.

Three research question were addressed:

Q1) What are the relationship between physical activity, functional capacity, and appetite in patients with heart failure?

Q2) How well do physical activity and functional capacity at baseline predict appetite at 18-month follow-up?

Q3) How do physical activity, functional capacity, and appetite change over time?

Methods

Study design and sample

This prospective observational study conformed with the principles outlined in the Declaration of Helsinki (21). It was approved by the Regional Ethical Review Board in

Linköping, Sweden (No M222-08/T81-09). The inclusion criteria were: age ≥ 18 years, diagnosed HF objectively confirmed by echocardiography with reduced ejection fraction (HFrEF), New York Heart Association (NYHA) functional classification II-IV, and able to read and write Swedish. Patients with kidney disease on dialysis, short life expectancy due to cancer and not being able to complete the data collection procedure were excluded, e.g., patients unable to visit the outpatient HF clinic for necessary assessments. Before the participants entered the study, written informed consent was obtained.

Procedure

Patients were recruited from three outpatient HF clinics in Sweden, led by HF nurses with significant experience of caring for patients with HF. A research nurse with extensive experience of caring for patients with HF, performing medical records reviews, and who was educated in performing the six minute walk test collected all study data. A consecutive sample of 316 patients was invited to participate in the study, of whom 186 (59%) accepted. Non-participants were significantly older than the participants [$t(313)=3.64$, $p<0.001$], but no gender differences were observed ($\chi^2(1)=0.10$, $p=0.701$). For those who accepted to participate, two study visits were scheduled within a week for baseline data collection. A first hospital visit was scheduled for clinical assessments, distribution of a questionnaire package to be completed at home, and for handing out a wearable metabolic-activity armband (actigraph) that participants were instructed to wear at home for 24 hours for 7 days. The second visit took place in the participants' home or in the hospital. On this occasion, questionnaires and the actigraph were collected.

To determine whether physical activity and functional capacity can predict appetite, participants were asked to complete a follow-up assessment after 18-months. This timepoint was chosen to observe the effects of HF progression. One hundred and sixteen (62.4%) of the

186 participants at baseline also completed the follow-up measures at the 18-month follow-up. There were no differences between those who completed the 18-month follow-up and the dropouts regarding gender, age, appetite and physical activity, However, the dropouts had significantly higher NYHA class at baseline ($\chi^2(2)=12.7, p=0.002$).

Measures

Appetite: The Council on Nutrition Appetite questionnaire (CNAQ) was used to measure self-reported appetite (22). The CNAQ consists of 8 items with 5 verbally ordered response alternatives. The total score ranges from 8-40, where CNAQ scores ≤ 28 indicate poor appetite with risk of significant weight loss ($\geq 5\%$) over a 6-month period (22). The Swedish version has shown sound psychometric properties regarding validity (item-total correlations, factor structure, construct validity, and know-group validity), and internal consistency (ordinal alpha) (2). In this study, internal consistency, estimated with Cronbach's alpha, was satisfactory ($\alpha=0.74$).

Physical activity: A numeric self-rating scale ranging from 1-10, where 1 indicates very low physical activity and 10 very high physical activity, were used to measure self-reported physical activity. Numeric rating scales have been widely used in pain and physical function assessments (23, 24). According to recommendations, the authors combined a self-reported assessment with direct assessment (25) by using a wearable multi-sensor actigraph (SenseWear®, Body Monitoring System) (26). The SenseWear® monitor measures different body physiological signals by four sensors; skin temperature, galvic skin response, heat flux sensor and 2-axis accelerometer. Based on these measurements, together with age, gender, height and weight, the SenseWear® monitor calculates daily physical activity, including total energy expenditure, active energy expenditure above 3 metabolic equivalents (METs), METs

daily average and number of steps. The METs correspond with an individual physical activity energy consumption and are calculated by Kcal/kg/hour. The METs were categorized as moderate physical activity 3-6 METs, moderate to vigorous >3 METs and vigorous >6 METs (27). All SenseWear measures for physical activity were calculated as mean values over the first four days, as all patients had valid measures for four days. The instrument has been validated among healthy individuals against doubly labelled water methods (28).

Functional capacity: Functional capacity was assessed with a six minute walk test. This test took place indoors in a quiet area at the hospital. Patients were instructed to walk up and down a 30-metre long corridor as rapidly as possible for 6 minutes. If any unpleasant symptoms occurred, such as breathlessness, fatigue or palpitations, the participants were advised to slow down to be as comfortable as possible, or terminate (29).

Heart failure severity: The New York Heart Association (NYHA) functional classification was used to classify heart failure severity by patients own narrative of which situations symptoms occurred: NYHA class I=no limitations of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations; NYHA class II=slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations; NYHA class III=Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in undue breathlessness, fatigue, or palpitations; NYHA class IV=Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased (30). B-type natriuretic peptide (BNP) was assessed specifically for this study at the first outpatient visit as indicator of HF severity.

Demographic and medical variables: Age and gender was self-reported. Medical variables, i.e., pharmacological treatment, duration of HF, left ventricle ejection fraction (EF), and comorbidity, were abstracted from medical records.

Data analysis

Sample characteristics, demographic and study variables are presented using descriptive statistics.

A series of linear regression analyses were conducted to investigate the relationship between physical activity, functional capacity and appetite at baseline (Q1). In a first step, physical activity and functional capacity was entered as explanatory variables, one model for each variable (i.e., self-reported physical activity, total energy expenditure, active energy expenditure, number of steps, METs daily average and the six minute walk test). In a second step, age, NYHA class, and BNP were entered as adjusting covariates.

To investigate whether physical activity and functional capacity were associated with appetite at the 18-month follow-up (Q2), the regression analyses were repeated, but with appetite from the follow-up assessment as the outcome variable.

Paired sample t-test was used to investigate changes in appetite, physical activity and functional capacity between baseline and the 18-month follow-up assessment (Q3).

A power calculation showed that a sample size of 85 participants would be sufficient to detect a medium effect for a multiple linear regression model including four explanatory variables, based on the following parameters; $f^2=0.15$, $1-\beta=0.8$ and $\alpha=0.05$. Additionally, a sample size of 34 participants would be sufficient to detect a medium effect size for an unpaired sample t-test, based on the following parameters; $d=0.5$, $1-\beta=0.8$ and $\alpha=0.05$. A medium effect size was used in these calculations as no previous study was identified, in which a suggested effect size was presented.

All statistical analyses were performed using IBM SPSS Statistics 20.0 (IBM Corp, Armonk, NY, USA). A p-value of <0.05 was considered statistically significant.

Results

Sample characteristics

The sample consisted of 186 patients with HF, 56 (30%) women and 130 (70%) men. The mean age was 70.7 (SD=11.0) years, and the majority (63%) had NYHA class II (range=II-IV). The mean body mass index (BMI) was 28.7 (SD=5.3) (Table 1).

Appetite and physical activity

A large number of the participants in the study reported poor appetite at the baseline assessment, with CNAQ scores ≤ 28 $n=71$ (38%). In general, the level of physical activity was low. At baseline, patients walked an average of 4,623 steps/day (SD=3,384,) and the METs daily average was 1.1 (SD=0.2). The walking distance averaged 370 meters (SD=144) in the six-minute walk test (Table 1).

Association between physical activity and appetite at baseline (Q1)

In the univariate models, higher levels of total energy expenditure ($b=0.150$, $p=0.041$), active energy expenditure ($b=0.175$, $p=0.017$), number of steps ($b=0.254$, $p<0.001$), METs daily average ($b=0.199$, $p=0.007$) and the six minute walk test ($b=0.266$, $p=0.001$) were significant associated with higher levels of appetite at baseline (Table 2). Physical activity and functional capacity explained 2-7% of the total variance in appetite, with walking distance in meters as the most important explanatory variable. In the adjusted models, number of steps ($b=0.204$, $p=0.019$) and the six minute walk test ($b=0.269$, $p=0.007$) remained significant associated with appetite (Table 2).

Physical activity as a predictor for appetite over time (Q2)

In the univariate models, self-reported physical activity ($b=0.207$, $p=0.026$), total energy expenditure ($b=0.196$, $p=0.035$), active energy expenditure ($b=0.220$, $p=0.018$), number of steps ($b=0.377$, $p<0.000$), METs daily average ($b=0.269$, $p=0.003$), and the six minute walk test ($b=0.254$, $p=0.010$) were significant predictors of appetite at 18-month follow-up (Table 3). Each of the physical activity variables explained 4-14% of the total variance in appetite, with number of steps as the most important explanatory variable. In the multivariate (adjusted) models, number of steps ($b=0.347$, $p=0.001$) and METs daily average ($b=0.206$, $p=0.040$) remained predictors of appetite at 18-month follow-up (Table 3).

Changes in physical activity and appetite over time (Q3)

No significant changes over time were shown for physical activity, functional capacity or appetite (Table 4).

Discussion

To our knowledge, this is the first study to investigate the relationship between physical activity, functional capacity, and appetite in patients with HF. Although the majority of the participants had mild to moderate HF symptoms (i.e., NYHA class II), the levels of physical activity and functional capacity were comparable to a sedentary lifestyle, which was consistent with previous studies (13, 14). Furthermore, appetite was low, indicating a risk of developing future weight loss (22). Low levels of physical activity and poor appetite are often described as a clinical concern among the most symptomatic patients with HF. These findings underline that low levels of physical activity and poor appetite are common problems in HF, even among those with less symptomatic HF.

The first research question sought to determine the relationships between physical activity, functional capacity and appetite in patients with HF. It was found that physical activity and functional capacity were associated with appetite in univariate regression models at baseline measurements. Of these associations, number of steps and the six minute walk test remained significant in the adjusted multivariate models. Our findings were similar with those of Saitoh et al., who found that HF patients with low appetite performed poorer on the six minute walk test in comparison with patients who did not experience loss of appetite (31). Our findings were also consistent with a study showing that the functional capacity of frail elders assessed by gait speed was significantly associated with appetite (3), implying that those who walked slower had poorer appetite.

The second research question was to determine how well baseline physical activity and functional capacity predicted appetite at the 18-month follow-up. It was found that all physical activity variables and functional capacity were significantly associated with appetite in univariate regression models at the 18-month follow-up, while in the adjusted multivariate models only number of steps and METS daily average remained significant. This result reflects the findings of a longitudinal study, which showed that loss of appetite predicts difficulties in performing daily physical activities, such as dressing and mobility at a two-year follow-up (3).

Just as in the study by Landin, the present study does not investigate the causal relationship between physical activity and appetite. Further studies are needed to determine whether there is a recursive relationship between these variables or if the relationship is non-recursive. After that, the causal direction needs to be confirmed. Independent of the relationship between the variables, physical activity and appetite should be recognized in patients with HF in clinical practice, both in hospitals and outpatient HF clinics.

Number of steps was an important variable to explain variations in appetite. This is contrary to a previous study that have showed no relationship between number of steps and appetite (32). This may be due to the present study investigating elderly patients with HF, whereas the previous study dealt with a small sample of younger health people. Increased number of steps is also found to be associated with a lower risk of cardiovascular events (33).

Although physical activity predicted appetite, neither appetite nor physical activity or functional capacity changed significantly over time. This finding was unexpected as HF is a progressive disease. Therefore, a deterioration in physical activity and appetite could have been expected. One likely explanation is that the participants who dropped out were the ones with the most severe HF symptoms, which was also supported by the dropout analysis.

Methodological considerations

A strength in the present study is the prospective design with a long-term follow-up, and the sample size. Even if the dropout rate was high, this was expected as prognosis is poor among patients with HF. This is supported by our dropout analyses, which show that significantly more participants with NYHA III and IV dropped out than those with NYHA II. However, the dropout rate will probably not affect the external validity as it was not possible to identify any differences in physical activity and appetite at baseline among those who completed the 18-month follow-up and those who did not. Despite the dropout, the sample was still large enough to conduct simple linear regression analyses.

Participants were instructed to wear the SenseWear armband for one week to average out daily variations. However, as a large share terminated before seven days, the first four days were used, independent on how long the participants had used the armband. All patients had sufficient valid data for the first four days and it was estimated to be enough to reflect daily variations.

The generalizability of the study findings is limited to outpatients with moderate-severe HF. In summary, the level of physical activity was low and appetite was poor in this study sample. Patients who were more physically active had better appetite, and these findings emphasize the importance of paying greater attention to physical activity and appetite jointly in clinical practice.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Implications for clinical practice

- The level of physical activity and appetite are important aspects to include in routine assessment of patients with heart failure since they are found to be affected in this population.
- Physical activity, such as walking, can possibly increase appetite. Therefore, health care professionals should pay attention to these components jointly as they might improve patients' health outcomes.

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Table 1. Participants' demographic and clinical characteristics

(N=186).

Age (years), mean (SD)	70.7 (11.0)
Female sex, n (%)	56 (30)
Duration of HF >5 years, n (%)	141 (76)
NYHA class, n (%)	
II	114 (61)
III	60 (32)
IV	12 (6)
LVEF, n (%)	
40-49	47 (25)
30-39	76 (40)
<30	63 (34)
BNP (qmol/l), mean (SD)	189.6 (195.2)
BMI (kg/m ²), mean (SD)	28.7 (5.3)
CCI, mean (SD)	1.8 (1.2)
Pharmacological treatment, n (%)	
Beta blocker	174 (94)
ACE-Inhibitor	111 (60)
Angiotensin receptor blocker	76 (41)
Aldosteron antagonist	63 (34)
Appetite	

CNAQ, mean (SD)	28.7 (3.5)
CNAQ \leq 28, n (%)	71 (38)
CNAQ > 28, n (%)	115 (62)
Physical activity	
Self-reported physical activity, mean (SD)	4.5 (1.8)
Total energy expenditure (kcal/day), mean (SD)	2208.5 (531.0)
Active energy expenditure (kcal/day), mean (SD)	228.2 (296.1)
Number of steps/day, mean (SD)	4623.0 (3384.3)
METs daily average/day, mean (SD)	1.1 (0.2)
Six minute walk test (meters/day), mean (SD)	369.5 (144.1)

ACE, angiotensin converting enzyme, BMI, Body mass Index;
 BNP, B-type natriuretic peptide; CCI, Charlson Comorbidity Index;
 CNAQ, Council on Nutrition Appetite Questionnaire; LVEF, Left
 Ventricular Ejection Fraction; METs, metabolic equivalents; NYHA
 class, New York Heart Association Classification; SD, standard
 deviation

Table 2. Association between physical activity, functional capacity, and appetite at baseline, based on univariate and multiple linear regression analyses.

	n	Step I – univariate linear regression			Step II – multiple linear regression		
		B ^a	b ^b	p-value	B ^a	b ^b	p-value
Self-reported physical activity	185	0.280	0.140	0.057	0.176	0.088	0.258
Age					-0.034	-0.107	0.178
NYHA					-1.045	-0.145	0.074
BNP					0.000	0.012	0.873
		F(1, 183)=3.668, p=0.057, R ² =0.020			F(4, 180)=2.674, p=0.034, R ² =0.056		
Total energy expenditure (kcal)	186	0.001	0.150	0.041	0.001	0.104	0.225
Age					-0.017	-0.055	0.530
NYHA					-1.245	-0.174	0.023
BNP					0.000	0.027	0.731
		F(1, 184)=4.250, p=0.041, R ² =0.023			F(4, 181)=2.697 p=0.032, R ² =0.056		
Active energy expenditure (kcal)	186	0.002	0.175	0.017	0.001	0.112	0.152
Age					-0.026	-0.083	0.297
NYHA					-1.058	-0.148	0.058
BNP					0.000	0.025	0.749

				F(1, 184)=5.790, p=0.017, R ² =0.031		F(4, 181)=2.850, p=0.025, R ² =0.059	
Number of steps	186	0.0003	0.254	<0.001	0.0002	0.204	0.019
Age					-0.014	-0.045	0.582
NYHA					-0.782	-0.109	0.171
BNP					0.001	0.046	0.560
				F(1, 184)=12.717, p<0.001, R ² =0.065		F(4, 181)=3.774, p=0.006, R ² =0.077	
METs daily average	186	3.422	0.199	0.007	2.332	0.136	0.083
Age					-0.027	-0.084	0.286
NYHA					-0.942	-0.132	0.097
BNP					0.000	0.014	0.853
				F(1, 184)=7.578, p=0.007, R ² =0.040		F(4, 181)=3.107, p=0.017, R ² =0.064	
Six minute walk test (meters)	155	0.006	0.266	0.001	0.006	0.269	0.007
Age					-0.010	-0.035	0.696
NYHA					-0.023	-0.003	0.971
BNP					0.001	0.063	0.454
				F(1, 153)=11.606, p=0.001, R ² =0.071		F(4, 150)=3.012, p=0.020, R ² =0.074	

B = unstandardized regression (slope) coefficient

b = standardized regression (slope) coefficient

BNP, B-type natriuretic peptide; NYHA class, New York Heart Association Classification; METs, metabolic equivalents

Table 3. Baseline predictors of appetite at 18-months, based on univariate and multiple linear regression analyses.

	n	Step I – univariate linear regression			Step II – multiple linear regression		
		B ^a	b ^b	p-value	B ^a	b ^b	p-value
Self-reported physical activity	116	0.373	0.207	0.026	0.283	0.157	0.110
Age					-0.025	-0.086	0.389
NYHA					-0.928	-0.138	0.166
BNP					-0.001	-0.053	0.588
		F(1, 114)=5.101, p=0.026, R ² =0.043			F(4, 111)=2.398, p=0.054, R ² =0.080		
Total energy expenditure (kcal)	116	0.001	0.196	0.035	0.001	0.152	0.145
Age					-0.002	-0.009	0.936
NYHA					-1.236	-0.184	0.052
BNP					-0.001	-0.048	0.630
		F(1, 114)=4.539, p=0.035, R ² =0.038			F(4, 111)=2.280, p=0.065, R ² =0.076		
Active energy expenditure (kcal)	116	0.003	0.220	0.018	0.002	0.154	0.118
Age					-0.016	-0.056	0.575

NYHA					-1.016	-0.151	0.121
BNP					-0.001	-0.43	0.667
				F(1, 114)=5.802, p=0.018, R ² =0.048		F(4, 111)=2.369, p=0.057, R ² =0.079	
Number of steps	116	0.0003	0.377	<0.001	0.0003	0.347	0.001
Age					-0.001	-0.003	0.979
NYHA					-0.547	-0.081	0.395
BNP					0.000	0.007	0.940
				F(1, 114)=18.888, p<0.001, R ² =0.142		F(4, 111)=4.813, p=0.001, R ² =0.148	
METs daily average	116	4.163	0.269	0.003	3.185	0.206	0.040
Age					-0.016	-0.054	0.582
NYHA					-0.793	-0.118	0.236
BNP					-0.001	-0.046	0.637
				F(1, 114)=8.907, p=0.003, R ² =0.072		F(4, 111)=2.855, p=0.027, R ² =0.093	
Six minute walk test (meters)	103	0.005	0.254	0.010	0.003	0.161	0.175
Age					-0.020	-0.69	0.514
NYHA					-0.931	-0.135	0.219
BNP					0.000	-0.031	0.771
				F(1, 101)=6.952, p=0.010, R ² =0.064		F(4, 98)=2.218, p=0.073, R ² =0.083	

B = unstandardized regression (slope) coefficient

b = standardized regression (slope) coefficient

BNP, B-type natriuretic peptide; NYHA class, New York Heart Association Classification; METs, metabolic equivalents

Table 4. Changes in appetite, physical activity and functional capacity between baseline and the 18-month follow-up assessment.

	n	Baseline, mean (SD)	18-month, mean (SD)	p-value ^a
Appetite (CNAQ)	116	28.9 (3.1)	28.5 (3.1)	0.054
Self-reported physical activity	116	4.7 (1.7)	4.6 (1.7)	0.723
Total energy expenditure (kcal)	101	2177.5 (495.7)	2129.0 (399.5)	0.172
Active energy expenditure (kcal)	101	218.2 (226.1)	192.1 (191.1)	0.178
Number of steps	101	4798.3 (3231.4)	4756.6 (3418.7)	0.830
METs daily average	101	1.101 (0.188)	1.080 (0.183)	0.095
Six minute walk test (meters)	85	405.3 (132.7)	412.8 (122.4)	0.446

a=Paired sample t-tests

CNAQ, Council on Nutrition Appetite Questionnaire