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ORIGINAL RESEARCH ARTICLE

Psychosocial factors, mental health, and coordination capacity in patients with heart failure with preserved ejection fraction compared with heart failure with reduced ejection fraction

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Abstract

Aims Patients with heart failure (HF) suffer from reduced quality-of-life (QoL). We aimed to compare QoL, depression, and anxiety scores among outpatients with preserved (HFpEF) and reduced (HFrEF) ejection fraction and non-HF controls and its relationship to coordination capacity.

Methods and results Fifty-five participants were recruited prospectively at the University Hospital Jena, Germany (17 HFpEF, 18 HFrEF, and 20 non-HF controls). All participants underwent echocardiography, cardiopulmonary exercise testing (CPET), 10 m walking test (10-MWT), isokinetic muscle function and coordination tests, and QoL assessments using the short form of health survey (SF-36), and hospital anxiety and depression scale (HADS). Furthermore, inflammatory biomarkers such as growth differentiation factor-15 (GDF-15) were assessed. Patients with HFpEF showed compared with HFrEF and non-HF controls reduced QoL [mental component score (MCS): 43.6 ± 7.1 vs. 50.2 ± 10.0 vs. 50.5 ± 5.0, P = 0.03), vitality (VT): 47.5 ± 8.4 vs. 53.6 ± 8.6 vs. 57.1 ± 5.2, P = 0.004), and elevated anxiety (6.5 ± 3.2 vs. 3.3 ± 2.8 vs. 3.8 ± 2. 8, P = 0.02) and depression scores (6.5 [3.5–10.0] vs. 3.0 [1.0–6.5] vs. 2.0 [0.75–3.0], P = 0.01)]. After adjusting to multiple comparisons, anxiety remained higher in HFpEF patients compared with HFrEF ($p_{post\text{-}hoc}$ = 0.009). HFpEF and HFrEF patients showed reduced coordination capacity compared with non-HF controls ($P < 0.05$). In a logistic regression, the presence of depression score ≥8 remained an independent factor for predicting reduced coordination capacity after adjusting for peak VO_2, GDF-15, 10-MWT, physical component score (PCS), and peak torque of the leg [odds ratio (OR): 0.1, 95% confidence interval (CI): 0.004–0.626, P = 0.02].

Conclusion Outpatients with HFpEF had worse QoL and higher anxiety and depression scores compared with HFrEF and non-HF controls. Depression is associated with reduced QoL and is an independent predictor for reduced coordination capacity.

Keywords Heart failure; Quality of life; Depression and anxiety; Coordination capacity

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Introduction

Heart failure (HF) is a major public health issue with steadily increasing incidence and prevalence. Hospitalization and mortality due to HF remain high in spite of advancements in the management of HF.[1,2] While advances in medical and device therapies have improved morbidity and mortality in patients with HFrEF, no benefits have been demonstrated in patients with HFpEF.[3–6] The only proven therapy so far to improve exercise capacity, dyspnoea, and QoL in patients with HFpEF is exercise training.[7] Patients with HF especially those with HFpEF suffer from exercise intolerance that not only impairs physical activity but also mental, psychological, and social life aspects in these patients.[8–10] Psychological and mental disorders such as depression and anxiety are common in both HFpEF and HFrEF[11,12] and have been proved to be independently associated with higher mortality and readmission rates.[10,13] Depression prevalence for example in patients with HF is 15–40%, and it increases the risk for morbidity and mortality.[14]

Recent studies focused on peripheral factors such as skeletal muscle in explaining the reduced exercise capacity, dyspnoea, and QoL.[15,16] One study in animal experiments showed a link between skeletal muscle dysfunction and depression.[17] Another group demonstrated that exercise training in HFpEF improves physical, psychological, and social components of QoL.[10] A further study in acute decompensated HF showed an association between physical function, cognitive dysfunction, and QoL.[18]

However, a systematic comprehensive comparison among clinically stable outpatients with HFpEF, HFrEF, and age-matched non-HF controls regarding QoL, depression, and anxiety and the relationship to coordination capacity and inflammatory biomarkers is still missing. We hypothesized that patients with HFpEF have worse QoL and increased prevalence of anxiety and depression compared with those with HFrEF and non-HF controls. Additionally, we investigated the link between QoL, depression, coordination capacity, inflammatory process, and muscle function in these patients.

Methods

Study population

Patients with HF were recruited from the HF outpatient clinic at the University Hospital Jena between September 2016 and June 2017. Non-HF controls were recruited from the general population in Jena and the neighboured cities. Altogether 55 subjects fulfilled our inclusion and exclusion criteria (17 HFpEF patients, 18 HFrEF patients, and 20 non-HF controls).

All subjects provided written informed consent at enrolment, and the protocol was approved by the responsible ethical review boards and fulfilled all principles of the Declaration of Helsinki.

Heart failure inclusion criteria

Clinically stable outpatients, men and women with age >55 years both with HFpEF and HFrEF and NYHA class II or III were recruited. HFpEF was defined as recommended by the European society of Cardiology-HF guidelines (ESC-HF).[19] Patients were on standard and stable HF medication for the last 3 months. Patients with HFpEF were further divided into groups according to phenotypes as suggested by Cohen *et al*.[20] The majority of our patients fulfilled the criteria of phenotype 2 and 3. According to Cohen *et al*., phenotype 2 was characterized by older age, highest proportion of women, a high prevalence of atrial fibrillation and chronic kidney disease, small concentric left ventricles with lowest left ventricle mass among the groups, as well as with the largest left atria, the lowest mitral annular tissue velocities, and the highest levels of inflammatory biomarkers related to the innate immune response (interleukin-8). On the other hand, phenotype 3 exhibited intermediate age, with a very high prevalence of obesity, diabetes mellitus, and remarkably impaired functional class, and the highest levels of biomarkers of tumour necrosis factor-mediated inflammation. These patients showed a distinct pattern of concentric left ventricular hypertrophy, with the highest values of left wall thickness, left ventricular mass, and left ventricular mass.

Heart failure exclusion criteria

Patients with major cardiovascular events or procedures in the last 6 weeks or patients with HF secondary to significant uncorrected valvular disease as well as patients with uncontrolled diabetes mellitus, progressive renal dysfunction (GFR < 60 mL/min) and those with primary muscle disorder such as muscular dystrophies were excluded.

Control subjects

Non-HF controls with a history of cardiovascular disease or other diseases except arterial hypertension and diabetes mellitus were excluded.

All subjects underwent a standardized series of assessments over two visits. Visit 1: Informed consent, DEXA scan, cardiopulmonary exercise test, echocardiography, and 6-min walk test. Visit 2: Muscle function/fatigability test, questionnaires, and blood tests.

Cardiopulmonary exercise testing

Exercise testing in association with air–gas exchange is considered to be an optimal gauge of functional capacity. We performed cardiopulmonary exercise testing (CPET) in all participants using incremental biking exercise on an electronically braked cycle ergometer.[21] Maximal O_2-uptake was abbreviated as PVO_2.

Questionnaire tools to complement functional assessment measurements

To assess measures of daily activity of patients with HF, we utilized several questionnaires that assess physical limitation, symptoms, and quality-of-life (QoL).

Visual analogue scale

Visual analogue scale is part of the European quality of life–5 dimensions (EQ-5D) questionnaire.[22] This questionnaire captures a self-rating of health status on a 20-cm vertical VAS, anchored at 100 (best imaginable health state) at the top and 0 (worst imaginable health state) at the bottom of the score. EQ-5D (VAS) ratings are a quantitative measure, and differences in this scale can be used as a measure of outcome, as judged by the individual respondents.[23,24]

The short form of health survey (SF-36)-assessment

SF-36 was performed as part of the QoL evaluations in all participants. This assessment consists of 36 items assigned to eight dimensions (physical functioning (PF), role limitation because of physical problems (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitation because of emotional health (RE), and mental health (MH). The eight dimensions were summarized in one score for mental (MCS) and physical (PCS) quality of life, respectively. We used a German translation of SF-36 with adapted norm values on German population.[25,26]

Hospital anxiety and depression scale

In order to perform a psychometric analysis and evaluate co-existing anxiety and depression, we asked the patients and the non-HF controls to fill in the HADS questionnaire.[27,28]

Dual-energy X-ray absorptiometry (DEXA) scan

A whole body DEXA scan was performed in all subjects to characterize the different compartments of soft tissue in the body. DEXA scanning is the most established method for the characterization of patients with advanced HF with a low radiation dosage and very low associated risks.[29] Appendicular lean mass was defined as the sum of muscle mass of arms and legs.

Muscle function by isokinetic dynamometry

The muscle function of the upper and lower extremities was assessed by the isokinetic dynamometry (CSMi Cybex HumacNorm®). A standardized measuring protocol was used to detect the parameters: (i) maximum muscle strength, (ii) muscle strength endurance, and (iii) muscular fatigue in the knee extension and knee flexion. The test protocol of the lower extremities included three different angular velocities in the concentric and eccentric mode was used. All values of the isokinetic measurement of the lower extremities were related to the muscle mass of legs unless mentioned otherwise.

i Maximum muscle strength

The participants were asked to perform five repetitions with the maximum force with the velocity of 60°/s (concentric knee extension and flexion), and 30°/s (eccentric knee extension and flexion). The best single attempt was defined as peak torque muscle strength. The higher the value, the better is the muscle strength.

ii Muscle strength endurance

The participants were asked to perform 15 repetitions with the maximum speed and to maintain it across the required performance. The velocity of the dynamometer was defined as 180°/s (knee extension and flexion). To detect the muscular endurance, the areas under the curves of every single attempt were summed. This outcome is equal to the physical work. The higher the value, the higher was the endurance and the higher the force level, which the participant was able to perform and maintain across the 15 repetitions.[30,31]

6 min walk test

Using standard methodology,[32] patients were asked to walk as fast as possible on a 25 m course for 6 min. The test was scored in rounded meters walked in 6 min.

Gait performance—10 m walk test (10-MWT)

A 10 m Walk Test was conducted to assess the gait speed of the individuals. The participants were asked to walk with a high velocity over 10 m in a straight line on a flat ground. The test was performed with a static start with a timed 10 m distance.[33,34]

Coordination capacity by dynamic balance

A straight-line walk test was used to detect the dynamic balance of the individuals. The participants were asked to

walk forward and backward along three different lines (2 m length, 25 cm, 20 and 15 cm line wide). This is a modified test from the previously published functional dynamic walking test by Lark *et al*.[35] In total, participants performed six single walks. As a result, the number of missteps (i.e. stepping with the entire foot beside the line = 1 point) was counted and compared among the groups.[36]

Serum analyses

Serum levels of GDF-15 and soluble urokinase-type plasminogen activator receptor (suPAR) were measured by using commercially available enzyme-linked immunosorbent assay (ELISA) kits (GDF-15: DY957, suPAR: DY807, R&D Systems, USA). Intra-assay variability and inter-assay variability were as follows: for GDF-15, 1.8–2.8%, 5.1–5.9% and for suPAR, 2.1–7.5%, 4.7–6%. Preparation of patient samples, assay reagents, and measurements was performed according to manufacturer's instructions based on previously published work. In short, patient samples and standard protein were added to the appropriate wells of the ELISA plates (Nunc MaxiSorp flat-bottom 96 well plates, VWR International GmbH, Austria), and plates were incubated for 2 h. ELISA plates were then washed using a Tween 20/PBS mix solution (Sigma Aldrich, USA). Afterwards, a biotin-labelled antibody was added and incubated for another 2 h. Plates were washed once more, and a streptavidin-horseradish-peroxidase solution was added to the wells. After another washing step and adding tetramethylbenzidine (TMB; Sigma Aldrich, USA), a colour reaction was achieved. This reaction was stopped by adding sulphuric acid. Values of optical density (OD) were determined at 450 nm on an ELISA plate-reader (iMark Microplate Absorbance Reader, Bio-Rad Laboratories, Austria).

Statistical analysis

All data and statistics are reported as mean ± standard deviation (n ± SD) for continuous normally distributed data or as median and interquartile range [25–75%] for variables that were not normally distributed, respectively. Categorical data were summarized by percentages. The χ^2 test was used to look for trend for categorical variables and Kruskal–Wallis test was applied for not normally distributed data, respectively. Analysis of variance (ANOVA), Pearson's, or Spearman simple regression were used as appropriate. Variables perceived as clinically important and those with $P < 0.1$ in univariate analyses were included in the multivariate model. A two-tailed P-value <0.05 or 0.0167 for *post hoc* comparisons indicates statistical significance. The Statistical Package for Social Sciences software (SPSS 26, IBM, Armonk, USA) was used for statistical analysis.

Results

Quality-of-life and mental health in heart failure

Basic characteristics are presented in *Table 1*.

To address different clinical phenogroups of patients with HFpEF, we provide here a summary of the clinical status of these patients.[20] There was only 2 (11.8%) patients <60 years old, 5 (29.4%) patients were obese (BMI > 30 kg/m^2), and only 2 (11.8%) patients had GFR < 60 mL/min. In general, similar to the suggested phenogroups by Cohen *et al*.,[20] the majority of our patients (12 patients) would fit the phenogroup 2: Age 72 ± 6 years old, 7 (58.3%) were women, and 7 (58.3%) had atrial fibrillation, E/e′ 13.2 ± 3.2, LAVI: 32.4 ± 6.5 mL/m^2. Further, 3 patients would match the phenogroups 3: [BMI: 36.7 ± 2.7 kg/m^2, 2 patients (66.6%) had NYHA III and 2 (66.6%) had diabetes mellitus].

Compared with HFrEF and non-HF controls, patients with HFpEF showed reduced mental component (MCS) and vitality (VT)-scores in the SF-36 questionnaire as well as elevated anxiety and depression scores in the HADS questionnaires (*Table 2* and *Figure 1A–D*). After adjusting to multiple comparisons and adjusting to sex and atrial fibrillation, anxiety remained higher in HFpEF patients compared with HFrEF ($p_{post\text{-}hoc}$ 0.009). As a result to the significantly different distributed gender among the three groups, we applied the same analysis on men only from the three groups and found that anxiety remains higher in male patients with HFpEF compared with HFrEF and non-HF controls (7.0 [5.0–9.0] vs. 2.0 [1.3–5.0] vs. 2.0 [1.5–5.5], P = 0.03). Compared with HFrEF and non-HF controls, female patients with HFpEF showed reduced vitality score (49.53 ± 3.52 vs. 62.30 ± 5.63 vs. 57.47 ± 5.21, P = 0.002). In a direct comparison to females with non-HF controls, women with HFpEF showed higher depression scores [(6.25 ± 3.33 vs. 2.64 ± 2.38, P = 0.02).

Coordination capacity and gait performance in patients with heart failure

Patients with HFpEF versus non-HF controls and HFrEF versus non-HF controls showed reduced balance and coordination capacities in the dynamic balance tests and in gait performance during 10-MWT (*Table 3*). There was no difference between HFpEF and HFrEF. Male patients with HFpEF compared with non-HF controls were slower in the 10-MWT (5.3 [5.0–7.0] vs. 4.9 [4.3–5.0] s, P = 0.007) and had reduced balance and coordination capacity in walking forward (FW-15: 2.0 [0.0–2.0] vs. 0.0 [0.0–0.0] misstep, P = 0.04). No difference was noted in this regard between HFpEF and HFrEF.

Table 1 Basic characteristics, co-morbidities and medications in patients with HFpEF, HFrEF, and non-HF controls

Characteristic	Non-HF controls $N = 20$	HFrEF $N = 18$	HFpEF $N = 17$	*P*-value
Age (years)	66 ± 7	68 ± 9	71 ± 6	0.17
Sex (m/f) f%	7/13 (65)	15/3 (17)**	8/9 (53)	0.009
BMI (kg/m^2)	26.4 ± 4.2	27.9 ± 5.3	28.7 ± 4.6	0.18
NYHA (II/III) %	(0/0)	(83.3/16.7)**	(76.5/23.5)*	<0.001
Left ventricle mass index (kg/m^3)	97.3 ± 22.7	165 ± 53.2**	152 ± 30.8*	<0.001
Left ventricle end-diastolic volume index (mL/m^2)	23.3 ± 2.6	28.6 ± 7.0**	24.9 ± 3.2***	0.004
Left ventricle ejection fraction (%)	61.0 [57.3–66.3]	30.0 [23.5–32.5]**	62.0 [53.0–66.0]***	<0.001
Left atrial volume index (mL/m^2)	17.2 ± 8.3	44.9 ± 19.0**	34.1 ± 7.1*	<0.001
E/e′	9.8 [8.1–11.8]	15.9 [13.9–24.5]**	13.1 [10.6–15.3]*	0.001
BNP (pg/mL)	35.5 [25.3–56.5]	317 [181–430]**	128 [73–218]***,*	<0.001
GFR (mL/min)	85.3 [70.9–94.3]	84.5 [60.1–94.4]	72.4 [67.5–82.2]	0.11
Acute myocardial infarct %	0 (0)	6 (33)**	5 (29)*	0.019
Hypertension %	10 (50)	15 (83)	15 (88)*	0.016
Diabetes mellitus %	2 (10)	7 (39)	6 (35)	0.091
Atrial fibrillation %	1 (5)	5 (28)	9 (53)*	0.005
ASS %	2 (10)	5 (39)**	7 (29)	0.004
Oral anticoagulation%	2 (10)	7 (39)	9 (53)*	0.017
Beta-blocker %	4 (20)	17 (94)**	13 (77)*	<0.001
ACEI/ARB/neprilysin inhibitor %	8 (40)	18 (100)**	12 (71) ***	<0.001
Aldosterone antagonist %	0 (0)	12 (67)**	3 (18) ***	<0.001
Diuretics %	6 (30)	16 (89)**	9 (53)	<0.001
Statins %	2 (10)	13 (72)**	11 (65)*	<0.001
Oral antidiabetic therapy %	0 (0)	4 (22)	5 (29)*	0.039

ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blocker; ASS, aspirin, BNP, brain natriuretic peptide; GFR, glomerular filtrating rate; NYHA, New York Heart Association.
*$P < 0.0167$ comparison between HFpEF and non-HF controls.
**$P < 0.0167$ comparison between HFrEF and non-HF controls.
***$P < 0.0167$ comparison between HFpEF and HFrEF.

Table 2 Quality of life in patients with HFpEF, HFrEF and non-HF controls

Parameters of quality of life	Non-HF controls $N = 20$	HFrEF $N = 18$	HFpEF $N = 17$	*P*-value
Physical functioning (PF)	58.2 [56.2–60.4]	50.9 [46.1–54.2]**	51.8 [43.7–55.3]*	<0.0001
Role limitation because of physical problems (RP)	56.8 [53.5–59.0]	48.0 [41.0–55.8]**	47.4 [42.4–51.6]*	0.002
Bodily pain (BP)	61.7 [54.3–63.3]	51.3 [39.6–62.1]	49.5 [38.7–60.1]*	0.01
General health (GH)	55.4 ± 9.8	46.1 ± 6.0**	47.2 ± 8.6*	0.006
Vitality (VT)	57.1 ± 5.2	53.6 ± 8.6	47.5 ± 8.4*, †	0.004
Social functioning (SF)	57.6 [55.7–58.3]	57.2 [43.8–57.8]	46.7 [44.8–50.2]*	0.002
Role limitation because of emotional health (RE)	55.5 [50.6–56.3]	53.9 [41.4–56.2]	48.9 [44.1–55.7]	0.08
Mental health (MH)	52.5 ± 7.0	50.2 ± 11. 7	45.2 ± 8.5	0.09
Physical score component (PCS)	56.3 ± 3.8	45.6 ± 5.9**	47.5 ± 8.3*	<0.0001
Mental score component (MCS)	50.5 ± 5.0	50.2 ± 10.0	43.6 ± 7.1*, †	0.03
EQ-5D (VAS)	85.0 [80–95.0]	65.0 [50.0–77.5]**	60.0 [50.0–72.5]*	<0.0001
HADS-Anxiety	3.8 ± 2. 8	3.3 ± 2.8	6.5 ± 3.2*,***	0.02
HADS-Depression	2.0 [0.75–3.0]	3.0 [1.0–6.5]	6.5 [3.5–10.0]*, †	0.01

Data from SF-36, EQ-5D, and HADS.
EQ-5D, European quality of life–5 dimensions; HADS, hospital anxiety and depression scale; VAS, visual analogue scale.
*$P < 0.0167$ comparison between HFpEF and non-HF controls.
**$P < 0.0167$ comparison between HFrEF and non-HF controls.
***$P < 0.0167$ comparison between HFpEF and HFrEF.
†$P < 0.05$ comparison between HFpEF and HFrEF.

Muscle function, mental health, and gait performance

The balance between knee concentric and eccentric movements is important to stabilize the gait and prevent against falls especially in elderly. We found that peak torque of knee in eccentric extension and after adjusting to sex was significantly lower in patients with HFpEF and HFrEF than in non-HF controls (151 ± 50.8 vs. 187 ± 39.7 vs. 220 ± 42.1 Nm/kg, $P = 0.02$). Furthermore, peak torque of right knee in eccentric flexion was associated with peak torque of right knee in concentric flexion was associated with ($r = 0.7$, $P < 0.0001$) and inversely with balance coordination capacity (walking backward on 15 cm wide line: r = −0.4,

Figure 1 Comparison of quality of life between HFpEF, HFrEF patients and non-HF controls. (A) Vitality (VT) as part of the SF-36-questionnaire. (B) Mental health component summery (MCS) as part of the SF-36-questionnaire. (C) Anxiety scale as part of the HADS-questionnaire. (D) Depression scale as part of the HADS-questionnaire. HADS, hospital anxiety and depression scale; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; MCS, mental health component summery; non-HF, non-heart failure; SF-36, short form of health survey; VT, vitality.

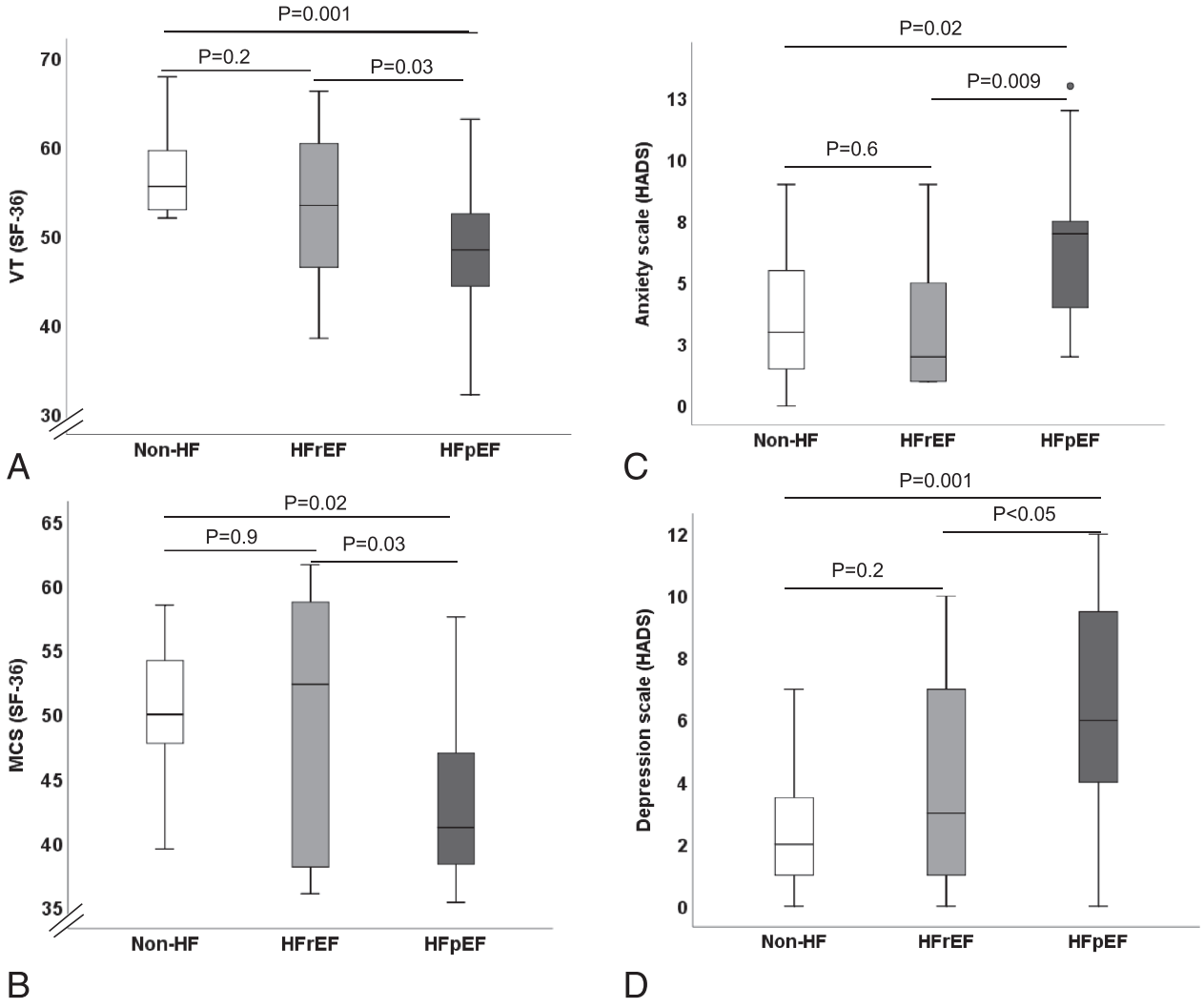

Table 3 Coordination capacity in patients with HFpEF, HFrEF, and age-matched non-HF controls

Measurements of coordination capacity	Non-HF controls $N = 20$	HFrEF $N = 18$	HFpEF $N = 17$	P-value
10-MWT (s)	4.9 [4.5–5.3]	5.3 [4.8–7.3]**	5.8 [5.0–8.3]*	0.003
Walking forward 20 cm	0.0 [0.0–0.0]	0.0 [0.0–0.0]	0.0 [0.0–0.3]	0.11
Walking forward 15 cm	0.0 [0.0–0.0]	0.0 [0.0–1.0]**	1.5 [0.0–3.0]*	0.01
Walking backward 20 cm	0.0 [0.0–1.0]	2.0 [1.0–3.0]**	2.0 [0.0–2.3]*	0.002
Walking backward 15 cm	1.5 [1.0–3.0]	3.0 [1.0–5.0]	4.0 [2.8–6.0]*	0.006

10-MWT, 10 m Walk Test.
*$P < 0.0167$ comparison between HFpEF and non-HF controls.
**$P < 0.0167$ comparison between HFrEF and non-HF controls.
***$P < 0.0167$ comparison between HFpEF and HFrEF.

P = 0.04). These correlations remained unchanged after adjusting to sex.

Patients with at least borderline anxiety (Anxiety in the HADS score ≥8) showed reduced QoL [(GH: 42.0 ± 6.5 vs. 49.7 ± 5.1), (VT: 43.8 ± 8.4 vs. 53.2 ± 7.2), (MH: 41.1 ± 9.1 vs. 49.2 ± 9.4), (VAS-score: 54.5 ± 12.1 vs. 72.8 ± 12.2, all $P < 0.05$)] (*Figure 2A,B*). Similarly, patients with at least borderline depression score in the HADS questionnaire (Depression in the HADS score ≥8) showed reduced coordination capacity (FW-15: 2.8 ± 3.0 vs. 0.9 ± 1.3 missteps, *P* = 0.03), and reduced several aspects of QoL [(MCS: 41.2 ± 4.8 vs. 49.2 ± 9.6, *P* = 0.04), (VT: 44.8 ± 7.5 vs. 52.2 ± 8.5, *P* = 0.04), (SF: 43.8 ± 7.8 vs. 51.0 ± 7.7, *P* = 0.02)] (*Figure 2C,D*). Similar results were shown by adjusting to sex among HFpEF, HFrEF, and non-HF controls.

In a logistic regression, the presence of at least borderline depression (≥8 points in the HADS questionnaire) remained an independent factor for predicting reduced coordination capacity in the dynamic balance tests (defined as number of missteps in walking forward on the 15-cm wide line ≥ mean value) after adjusting for peak VO2, GDF-15, 10-MWT, PCS, and peak torque of the right leg in extension [odds ratio (OR): 0.1, 95% confidence interval (CI): 0.004–0.626, *P* = 0.02] (*Table 4*).

Inflammatory biomarkers and their relation to muscle function, coordination capacity, and quality of life

Patients with elevated GDF-15 (> mean value) showed reduced coordination [(walking backward 20 cm: 2.6 ± 1.8 vs. 1.3 ± 1.4 misstep), (walking forward 15 cm: 2.4 ± 2.7 vs. 0.9 ± 1.3 misstep, all $P < 0.05$)]. Additionally, patients with

Figure 2 The influence of depression and anxiety in patients with HF on QoL. (A) Reduced mental health (SF-36) patients with at least borderline anxiety score. (B) Reduced QoL measured by VAS-score in patients with at least borderline anxiety score. (C) Reduced mental health (SF-36) in patients with at least borderline depression score. (D) Reduced social functioning (SF-36) in patients with at least borderline depression score. EQ-5D, European quality of life–5 dimensions; VAS-score, visual analogue scale.

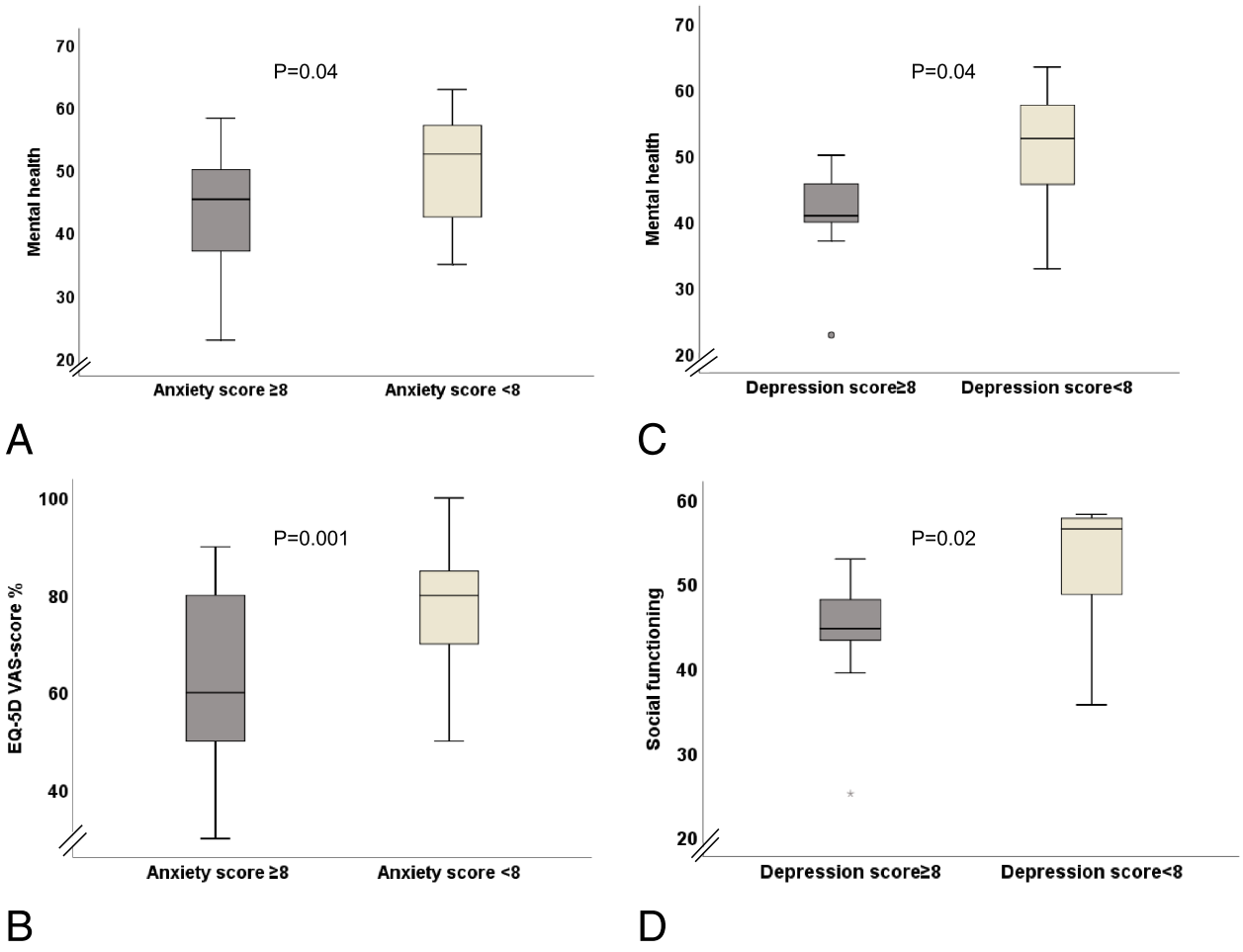

Table 4 Logistic regression model with reduced coordination capacity estimated in walking forward on 15-cm-wide line (< mean value of the cohort) serving as the dependent variable

	Univariate			Multivariate		
Variable	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Age (per year increase)	1.1	0.97–1.13	0.2			
Sex (male/female)	2.3	0.72–7.11	0.2			
Peak VO2 (per 1 mL/kg/min increase)	0.9	0.74–0.97	0.02	1.2	0.86–1.71	0.3
Peak torque of right leg in extension (per 1 Nm/kg increase)	0.8	0.65–0.99	0.04	0.7	0.44–1.17	0.2
GDF-15 (per 1 pg/mL increase)	1.0	1.00–1.01	0.01	1.0	1.00–1.01	0.2
Depression score ≥8 (present)	0.1	0.01–0.41	0.006	0.1	0.004–0.63	0.02
PCS (per 1-point increase)	0.9	0.83–0.99	0.04	0.9	0.76–1.04	0.1
10-MWT (per 1 s increase)	1.4	0.96–1.96	0.08	0.9	0.42–1.98	0.2

GDF-15, growth differentiation factor-15; 10-MWT, 10 m walking test; PCS, physical component score of the SF-36 questionnaire; Peak VO_2, maximal oxygen consumption.

elevated suPAR (> mean value) showed reduced QoL in different aspects of SF-36 [(GH: 43.5 ± 6.1 vs. 49.3 ± 7.4), (SF: 45.3 ± 9.2 vs. 51.7 ± 6.4), (RE: 45.1 ± 7.7 vs. 52.4 ± 4.2), (MH: 42.9 ± 9.6 vs. 51.5 ± 9.3), (MCS: 41.9 ± 7.2 vs. 50.2 ± 8.8, all $P < 0.05$)]. The aforementioned results (GDF-15 and suPAR) remained unchanged after adjusting to sex.

Discussion

We showed for the first time to our knowledge in clinically stable outpatients with HF a profound reduction in QoL in patients with HFpEF assessed by mental health and vitality in the SF-36 questionnaire and increased anxiety and depression scores in the HADS questionnaire compared with those with HFrEF and non-HF controls. Both HFpEF and HFrEF showed reduced coordination capacities compared with non-HF controls. Elevated levels of inflammatory biomarkers were associated with reduced QoL and impaired coordination capacity. In a logistic regression the presence of at least borderline depression (≥8 points in the HADS questionnaire) remained an independent factor for predicting reduced coordination capacity in the dynamic balance tests after adjusting for peak VO2, GDF-15, 10-MWT, PCS, and peak torque of the right leg in extension.

The main symptoms in patients with HF are exercise intolerance and fatigue. Peripheral factors such as skeletal muscle dysfunction seem to play an important role in explaining exercise intolerance and reduced QoL in these patients.[15,37] In spite of the proven reduced QoL in patients with HF in different aspects such as social, emotional and cognitive fields,[8,10] the evaluation and management of QoL in these patients are not included in the daily practice and still considered to be a gap in the management of patients with HF.[38]

Quality of life and psychosocial factors

A couple of studies compared QoL (SF-36) in patients with HFpEF and HFrEF[39–41] and found similar reduction in QoL between these two groups. This is likely due to using different definitions for making the diagnosis of HFpEF than the currently recommended one from the ESC-HF.[19]

Recently, it has been shown in acute decompensated HF patients that patients with HFpEF defined according to the current recommendations of the ESC-HF guidelines[19] had higher rates of depression than those with HFrEF.[42] Our findings are in line with this showing increased anxiety and depression scores in the HADS questionnaire compared with those with HFrEF and non-HF controls. In addition, patients with higher depression scores had worse coordination and balance capacity, and reduced QoL demonstrated in the SF-36-questionnaire by reduced vitality, social function, and mental component score.

Inflammatory biomarkers and quality of life

An elevation of GDF-15 in patients with HF is known as well.[43,44] However, we described in the current study the relationship between inflammatory biomarkers and coordination capacity and QoL. Patients with elevated GDF-15 had reduced coordination capacity in the balance tests. Those with elevated levels of the inflammatory biomarker suPAR had reduced QoL in several aspects of SF-36-questionnaire such as general health, social function, and mental health. These results should be confirmed in larger studies and the pathophysiology needs to be investigated.

Physical evaluation and dynamic balance

Muscle strength and the balance between knee concentric and eccentric movements as well as the speed of developing peak torque are important factors to stabilize the gait and prevent against falls especially in elderly.[45–49] Furthermore, the muscular activation pattern during concentric and eccentric isokinetic movements seems to be different with a higher frequency of motor units during the eccentric muscle performance.[50] This emphasizes the importance of

eccentric movements of the knee in creating higher strength and as a result ensuring more gait balance. Our findings are supportive in this regard. We found that coordination capacity and peak torque of knee in eccentric extension were significantly lower in patients with HFpEF and HFrEF than in non-HF controls. In addition, there was a correlation between 'the reduced' muscle strength especially in eccentric movements of the knee and balance dynamic tests. This all makes patients with HF more susceptible to falls and to the following health-related, social, and economic consequences and emphasizes the importance of normal muscle function in stabilizing gait performance and improving coordination capacity.

In conclusion, clinically stable outpatients with HFpEF have worse QoL and elevated prevalence of anxiety and depression compared with those with HFrEF and non-HF controls. Depression was associated with reduced QoL and is an independent predictor for reduced coordination capacity.

While our results need to be confirmed with larger cohorts of patients, screening for reduced QoL should be included in our daily practice in the management of patients with HF.

Limitations

Our study was performed on small number of participants. Additional limitation remains the baseline differences (sex distribution, atrial fibrillation, and BNP). Although we addressed this issue by performing an analysis adjusted to these factors, the small sample volume remains a main limitation to this analysis. Therefore, larger studies are required to confirm our results.

Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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