

Validation of the FEW16 questionnaire for the assessment of physical well-being in patients with heart failure with reduced ejection fraction: results from the CIBIS-ELD study

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Abstract

Aims Patients with heart failure (HF) commonly suffer from severe impairment of quality of life (QoL). One main goal of HF treatment is improvement of QoL. Physical well-being is an essential component of QoL. To enable assessment of physical well-being in HF patients, we validated the FEW16 questionnaire in a prospective study with patients from the Cardiac Insufficiency Bisoprolol Study in ELDerly.

Methods and results In 127 HF patients (age 73±5.5 years, 72% male, 60% New York Heart Association class II, left ventricular ejection fraction 37±8.5%), we measured physical well-being (FEW16), QoL [36-Item Short-Form Health Survey (SF36)], and depressive symptoms [PRIME MD Patient Health Questionnaire German short version for depression (PHQ-D)] at baseline and two follow-up visits, and correlated FEW16 scores with QoL data and clinical parameters. FEW16 mean scores are 3.04±1.04 at baseline, 3.19±0.94 after 3 months, and 2.77±0.94 after 2–4 years. We assessed data quality, scale assumptions, and construct validity and reliability. Cronbach's alpha for subscales resilience: 0.84; ability to enjoy: 0.80; vitality: 0.88; inner peace: 0.87; total score: 0.95. Intraclass correlation coefficient (ICC) is 0.87 (95% CI 0.84–0.89, ICC (1.4). Pearson's correlations of FEW16 with SF36 and PHQ-D were significant. Six minutes walking distance and heart rate correlated significantly with the FEW16 total score.

Conclusions The FEW16 showed good reliability, internal consistency, and intraclass correlation. FEW16 scores correlated well with psychological and physical well-being (SF36) and clinical markers of exercise tolerance (6 min walk test and heart rate). Our results indicate a strong correlation of self-reported physical well-being with psychological factors. FEW16 values at baseline predicted the development of several aspects of QoL during beta-blocker up-titration.

Keywords Heart failure; FEW16; Physical well-being; Quality of life (QoL); Validation

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Introduction

Heart failure (HF) is a globally growing health problem with high rates of mortality and morbidity and associated with considerable impairment in quality of life (QoL). In westernized countries, HF is the most common cause for hospitalization in patients above age 65 years,¹ rendering HF one of the principal burdens for health care systems in the 21st century.² Besides morbidity and mortality, QoL has been identified as one major patient-reported outcome (PRO),³ and poor QoL in HF has been associated with reduced survival.^{4–6}

Patient's health status significantly impacts on QoL, which includes mental, physical, and social aspects of life. Impairment of QoL through illness may lead to depression, social isolation, and diminished adherence to therapy.^{7,8} On the other hand, the potentially causal associations are bi-directional: treatment itself (e.g. betablocker therapy) may affect QoL, and 'objective clinical improvement' may differ from the 'subjective well-being' of patients.

The European Society of Cardiology emphasizes the necessity to study PROs as endpoints in clinical studies because—from a patient perspective—they bear similar relevance compared with morbidity and mortality and may thus be regarded complementary endpoints.⁹ Disease management in HF should be directed not only to prolong life but also to enhance the patient's well-being and QoL. In this respect, PRO data reflecting the subjective experience of treated patients may serve well in the decision-making process of the therapeutic strategy.

Ideally, a self-report by the patient should serve several purposes: help the caring team in the patient assessment, assure the patient that he or she is being perceived as an individual in a holistic treatment approach, and raise patient's awareness about his or her health condition. However, the clinical utility of a patient questionnaire not only depends on the number and phrasing of questions, but also on the subject's general condition present when filling in the questionnaire. In patients with HF, comorbid conditions (e.g. depressed mood) have major confounding role.^{7,10,11} It is thus important to validate questionnaires for use in specific subpopulations and to include the knowledge and input of those patients into its design process.

The aim of the presented work was to further validate the questionnaire for subjective physical well-being (FEW16 - Fragebogen für die Erhebung des körperlichen Wohlbefindens) for its use in patients with systolic HF.

Methods

Ethical approval of the study and informed consent

The investigation conforms to the principles outlined in the Declaration of Helsinki. The German Health Authorities and the Ethics Committees at each centre approved the study.

Written informed consent was obtained from all patients prior to any study-related procedures.

Study population

For the current report we sampled 136 patients from the Cardiac Insufficiency Bisoprolol Study in ELDERly (CIBIS-ELD) study, a randomized prospective trial investigating the differential impact of betablockers in elderly patients with heart failure with reduced (or preserved) left ventricular ejection fraction (LVEF). The study design has been reported in detail elsewhere.¹² Briefly, eligible patients were ≥ 65 years of age, diagnosed with symptomatic HF (i.e. NYHA functional class \geq II) or LVEF $\leq 45\%$ and had stable symptoms in the last 2 weeks prior to inclusion. After obtaining written consent for this study, we measured the physical and psychological well-being by use of the FEW16 as well as the QoL [36-Item Short-Form Health Survey (SF36)] and depressive symptoms [PRIME MD Patient Health Questionnaire German short version (PHQ-D)].

Data collection and instruments

We collected data at trial baseline (i.e. the start of beta-blocker up-titration) and after 3 months of follow-up (FU1). Additional data were collected 2 to 4 years after baseline (FU2) to gather longitudinal information. All questionnaires were completed by the patients themselves in the outpatient department without supervision.

FEW16

In order to adapt this concept of salutogenesis by Aaron Antonovsky, Kolip & Schmidt developed the FEW16, a 16-item 'Questionnaire for assessing Physical Well-being', with a particular emphasis on positive phrasings, because previous questionnaires rather focused on inabilities and pain.¹³ The FEW16 measures the subjective habitual physical well-being through the last 3 weeks by concentrating on the psychological well-being in the sense of affective experiencing¹⁴ and abilities rather than on the absence of disease, pain, or physical incapacity.^{15,16} The habitual well-being is perceived as a construct, which is relatively stable over weeks to months. It relies on the assessment of emotional experiences and is thus influenced by also stable personality traits and the subject's environment.¹⁷ The FEW16 questionnaire has been validated using two patient populations from a rehabilitation centre and one sample population of healthy university students.¹³ Albani *et al.* 2006¹⁸ applied the FEW16 in healthy samples of 573 subjects from East and 1900 subjects from West Germany. Their results speak for a good reliability and internal consistency of the FEW16 questionnaire.

The FEW16 consists of four subscales: *Resilience*, *Ability to Enjoy*, *Vitality*, and *Inner Peace*, each of which contains four items. The items are to be answered on a 6-point Likert scale

with answer options ranging from 'fully applies' (yielding 5 points) to 'does not apply at all' (yielding 0 points). Higher scores indicate better physical well-being. The subscale values are calculated as mean of the values for the four subscale items. Per subscale, a maximum of one erroneous value can be substituted by the mean of the subscale. The total score is calculated as the mean of the four subscale values. High values stand for good physical well-being.

36-Item Short-Form Health Survey

To estimate the construct validity of the FEW16, we used the German version^{19,20} of the MOS 36-Item Short-Form Health Survey (SF36) by Ware & Sherbourn,²¹ which is a standard questionnaire for the assessment of health-related QoL. The employed version concentrates on the period throughout the last 4 weeks. The SF36 consists of 36 items assigned to eight subscales assessing the following aspects of health: *Physical Functioning, Role Physical, Role Emotional, Pain, Social Functioning, Mental Health, Vitality, and General Health Perceptions*. The questions are to be answered on 3-point, 5-point or 6-point Likert scales or on a yes or no basis. The answers are transformed into scores which range from 0 for 'poorest' to 100 for 'best possible QoL'. In addition, two superordinate scores are calculated by combination of items, one of which is related to physical health, the other to mental well-being. The questionnaire is completed in 5 to 10 min. The German version of the SF36 has been extensively validated by several studies^{22–31} and is itself employed for the validation of newer disease-related questionnaires.^{32,33}

PRIME MD Patient Health Questionnaire German short version

The PHQ-D questionnaire was designed for the recognition of the main psychological symptoms in primary medical care,³⁴ originally developed as 'PRIME MD Patient Health Questionnaire (PHQ)'.³⁵ For this study, we used the authorized German version of the questionnaire's short version for depression (PHQ-D,³⁶) consisting of nine questions to assess depressive symptoms in patients. The questions ask how often the patients suffer from different types of discomfort on a scale ranging from '0' ('not at all') to '3' ('almost every day'). The points from all questions are summed up, yielding a score that indicates no depression/healthy (<5), mild or subliminal depression,^{6–9} or major depression with the distinction of medium,^{10–14} pronounced,^{15–19} or severe.^{20–27} The PHQ-D questionnaire can be answered quickly, is easy to interpret, and has been recognized as valid and reliable.^{37–39}

Statistical analysis

Baseline characteristics are described using mean ± SD or *n* (%). The first step of analysis was a revalidation of the FEW16. In order to examine the factorial structure, a principal component analysis with varimax rotation was used, analogous to the original instrument development.¹³ As a measure

of internal consistency, intraclass correlations (type 3), Cronbach's alpha coefficient and Guttman's lambda6 were calculated. Probability of answering levels per item was estimated via the 25th/75th percentile. For a cross-validation with the SF36 questionnaire and the PHD-Q, Spearman rank correlations were calculated.

The second step of analysis focused on the relations between physical well-being and clinical parameters. Spearman rank correlations were calculated for quantitative values such as the distance in the 6 min walking test (6MWT). For categorical data such as sex or NYHA category, the groups were compared using the Kruskal–Wallis rank sum test. In addition to the baseline values of the patients, their changes at a follow-up examination after 4 years were analyzed in order to test the possible prognostic value of the FEW16 scales.

In an exploratory fashion, all correlations were calculated separately for the gender groups after the analysis in the total sample. A formal comparison between the groups by means of inferential statistics was not part of this analysis and would require a greater sample size.

Five per cent was defined as the level for statistical significance. All calculations were made in the statistical scripting language R (<http://www.R-project.org/>).

Results

Patient sample

Only patients diagnosed with systolic HF were recruited for this study (LVEF ≤ 45%, *n* = 136). For 127 of those patients, complete data were available at baseline and thus used for final analysis [mean age 73 ± 5.5 years, 72% male, mean LVEF 37 ± 8.5%, and 5.5%, 59.8%, and 34.7% in NYHA functional class I, II, and III, respectively (*Table 1*)]. Due to some missing data, we have complete FEW16 and SF36 data for the follow-up after 3 months for 118 patients and for the follow-up after 2–4 years for 44 patients which could be included into the calculations. When calculating changes between data from different time points, we applied pairwise tests, including only patients with valid data at both measurement times.

FEW16, 36-Item Short-Form Health Survey, and PRIME MD Patient Health Questionnaire German short version questionnaires

Figure 1 shows the scores of all questionnaires at the different time points. The FEW16 total score increased significantly from 3.04 ± 1.04 at baseline to 3.19 ± 0.94 at FU1. At FU2, the total score had decreased to 2.77 ± 0.94 (*P* = n.s. compared with baseline). Regarding the subscales, the scores for *Ability*

to *Enjoy* and *Vitality* increased significantly from baseline to FU1, but changes to FU2 were not significant. Values for all SF36 subscales significantly increased between baseline and FU1. At FU2, scores for *General Health perceptions*, *Role Emotional*, and the psychological component score had increased, and *Role Physical* had decreased significantly. We further detected a significantly reduced total score for the PHQ-D at FU1 when compared with baseline, which returned back to baseline levels at FU2.

Factorial structure and internal consistency

The factorial structure of the FEW16 questionnaire showed four factors (Figure 2). Items 1, 5, 8, and 10 are originally assigned to subscale *Resilience* (PA3). In our dataset, item 8 had a strong relationship to this subscale with a factor loading of 0.47, but was equally related to the scale *Ability to Enjoy* with a factor loading of 0.48. Because of the numerically

Table 1 Medical description of the sample all at time points

Parameter	Baseline	3 months	2–4 years
Age mean \pm SD (years)	73 \pm 5.5		
Sex male/female (%)	72/28	72/28	72/28
BMI (kg/m ²) \pm SD	27.9 \pm 4.5		28.8 \pm 4.6
Drinks per week mean \pm SD	1.41 \pm 3.7		
6 min walking distance \pm SD (m)	356 \pm 114	364 \pm 109	340 \pm 148
Left ventricular ejection fraction mean \pm SD	37 \pm 8.5	41 \pm 10.2	
NYHA 1/2/3/4 (%)	5.5/59.8/34.7	15.8/67.7/16.5	27/57/13/3
Myocardial infarction (%)	46		8
Biventricular pacemaker no/yes (%)	98/2		97/3
Hypertension (%)	88		
Adipositas (%)	30		
Diabetes mellitus (%)	26		
Hyperlipidemia (%)	75		
Non-smoker/ex-smoker/smoker (%)	52/40/8		
Ace inhibitor (%)	76	69	69
Betablocker (%)	58	80	80
Glykosides (%)	17	9	9
Aldosterone antagonists (%)	23	18	18
Nitrite (%)	34	25	25
Statins (%)	52	52	52
Aspirin (%)	69	73	73

SD, standard deviation; NYHA, New York Health Association.

Figure 1 Mean scores of FEW16, 36-Item Short-Form Health Survey (SF36) and PRIME MD Patient Health Questionnaire German short version (PHQ-D) at all three time points with standard errors. Stars indicate significant difference to baseline. $n = 127$ at baseline, $n = 118$ at after 3 months (FU1), $n = 44$ at 2 to 4 years after baseline (FU2). Pairwise calculation of change significances. * $P < 0.001$, ** $P < 0.01$, * $P < 0.05$.**

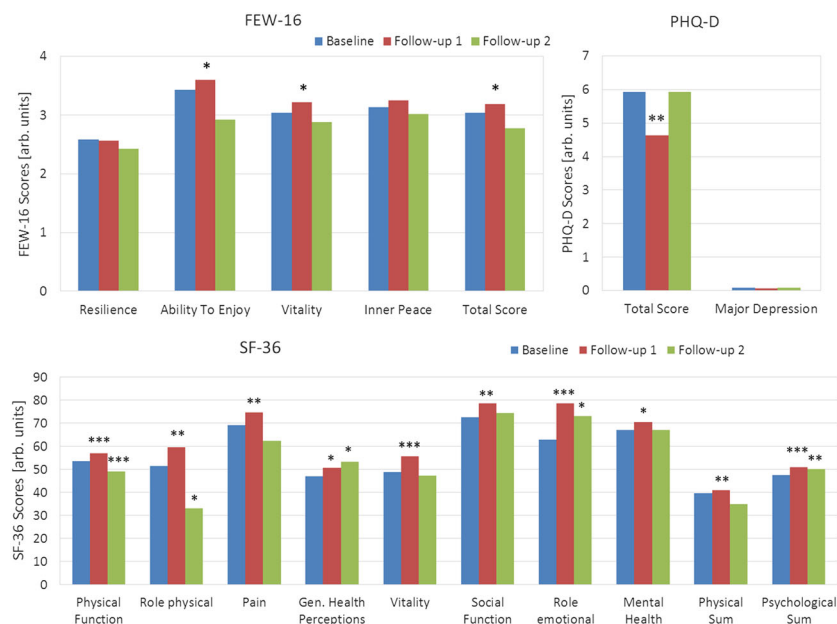
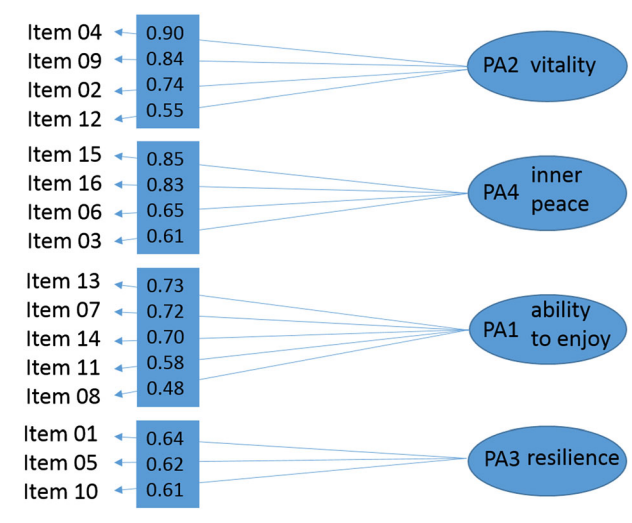


Figure 2 Factorial structure with factor loadings of the FEW16 items as found in the present study.



slightly higher value for *Ability to Enjoy*, item 8 would be assigned to this subscale. Items 7, 11, 13, and 14 were assigned to the subscale *Ability to Enjoy* (PA1) as expected, and the subscales *Vitality* (PA2, items 2, 4, 9, and 12) and *Inner Peace* (PA4, items 3, 6, 15 and 16) were successfully replicated as well. These four factors explained about 70% of the variance of the 16 items. The scale values for the Cronbach's alpha coefficient are between 0.84 and 0.91 and, thus, substantially larger than the commonly advocated threshold of 0.4 to 0.7 for sufficient reliability. Guttman's lambda6 values between 0.83 and 0.91 indicated good internal consistency in the subscales (Table 2).

Construct validity—correlation of FEW16 with 36-Item Short-Form Health Survey and PRIME MD Patient Health Questionnaire German short version subscales at baseline

Table 3 presents the correlations of the FEW16 with the SF36 and PHQ-D subscales. Overall, the FEW16 showed significant positive correlations both with the total score and all subscales of the SF36. The FEW16 total score showed the highest correlations with the SF36 subscales *Vitality* and *Mental Health*. We

found the strongest correlations of SF36 *Vitality* for FEW16 *Ability to Enjoy* and *Vitality*. Interestingly, the FEW16 total score showed a stronger correlation with the psychological than with the physical component score of the SF36. The psychological component score had the highest correlation with the *Inner Peace* subscale, almost as strong as with the FEW16 total score. The physical component scale correlated best with FEW16 *Vitality*. The correlations of the FEW16 scores with those of the PHQ-D were all significant and negative. They were strongest for the PHQ-D subscales *Difficulties sleeping*, *Feeling tired/having little energy*, and *Feeling down, depressed, hopeless*. Here, *Difficulties sleeping* was most strongly related to FEW16 *Vitality*. *Feeling tired/having little energy* correlated most strongly with *Ability to enjoy* as did *Little interest/pleasure in doing things* and *Poor appetite/overeating*. The PHQ-D subscales *Thoughts of suicide*, *Physical impairments*, *Lack of self-confidence*, and *Difficulties concentrating* all correlated most strongly with FEW16 subscale *Inner Peace*.

Relation between clinical measurements and FEW16 and presumed gender specificity

Table 4 shows the correlations between clinical data and FEW16 scales. We found significant correlations between the 6MWT and the FEW16 total score (0.24) as well as with the subscales *Resilience* (0.26), *Inner Peace* (0.21), and *Ability to Enjoy* (0.18). In addition, patients' heart rate showed significant negative correlations with the FEW16 total score (−0.22) and with the subscales *Ability to Enjoy* (−0.22) and *Resilience* (−0.20). A tendency was found for *Inner Peace* and heart rate. Age and LVEF on the other hand did not correlate with any of the FEW16 scales. As for sex, NYHA class, and betablocker therapy, there were no significant correlations with any FEW16 scale either, although tendencies were noted for a correlation between sex and *Vitality*, *Inner Peace* and the total FEW16 score, and for NYHA class and *Resilience*. Major depression correlated significantly with all subscales and with the total FEW16.

Figure 3 shows the potential impact of gender on the relations between FEW16 scales and clinical measurements using the 6MWT as an example. There was a positive relationship between physical well-being (total score FEW16) and the 6MWT, which was detectable in men only.

Table 2 Statistical key figures of the FEW16 subscales at baseline

Scale	Median	25th/ 75th percentile	Relative part of total variance	Cronbach's Alpha	Guttman's lambda6	Intercorrelation coefficient type 3	ICC3 confidence interval
Resilience	2.5	1.8/3.5	0.188	0.836	0.828	0.561	0.476/0.644
Ability to Enjoy	3.5	2.8/4.5	0.202	0.878	0.858	0.642	0.565/0.714
Vitality	3.2	2.0/4.0	0.123	0.914	0.911	0.728	0.663/0.786
Inner Peace	3.2	2.5/4.0	0.194	0.900	0.897	0.692	0.622/0.757

Table 3 Correlation coefficients of FEW16 subscales with the subscales of 36-Item Short-Form Health Survey and the PRIME MD Patient Health Questionnaire German short version instruments at baseline

Variable	Resilience	Ability to Enjoy	Vitality	Inner Peace	FEW16
SF36					
Vitality	0.666***	0.727***	0.713***	0.628***	0.801***
Mental Health	0.504***	0.627***	0.532***	0.756***	0.703***
Social Functioning	0.491***	0.471***	0.449***	0.534***	0.551***
General Health Perceptions	0.514***	0.439***	0.443***	0.495***	0.543***
Role—Physical	0.452***	0.454***	0.519***	0.342***	0.514***
Physical Functioning	0.460***	0.467***	0.455***	0.384***	0.501***
Pain	0.406***	0.403***	0.444***	0.433***	0.474***
Role—Emotional	0.295**	0.311***	0.382***	0.325***	0.385***
Physical, sum	0.435***	0.418***	0.476***	0.304***	0.469***
Psychological, sum	0.466***	0.541***	0.540***	0.620***	0.634***
PHQ-D					
Difficulties sleeping	-0.461***	-0.576***	-0.627***	-0.420***	-0.618***
Feeling tired or having little energy	-0.501***	-0.567***	-0.549***	-0.412***	-0.600***
Feeling down, depressed or hopeless	-0.458***	-0.517***	-0.449***	-0.556***	-0.573***
Little interest or pleasure in doing things	-0.455***	-0.477***	-0.392***	-0.401***	-0.510***
Thoughts of suicide	-0.390***	-0.437***	-0.413***	-0.529***	-0.496***
Physical impairments	-0.397***	-0.434***	-0.383***	-0.487***	-0.469***
Lack of self-confidence	-0.332***	-0.425***	-0.370***	-0.495***	-0.455***
Difficulties concentrating on things	-0.298***	-0.435***	-0.323***	-0.459***	-0.438***
Poor appetite or overeating	-0.238**	-0.410***	-0.270**	-0.342***	-0.365***

*** $P < 0.001$, ** $P < 0.01$.

SF36, 36-Item Short-Form Health Survey; PHQ-D, PRIME MD Patient Health Questionnaire German short version.

Table 4 Correlation coefficients of the FEW16 subscales with clinical parameters at baseline

Variable	Resilience	Ability to Enjoy	Vitality	Inner Peace	FEW16
Age	-0.042	-0.112	-0.083	-0.011	-0.086
6 min walking distance	0.256 **	0.180 *	0.139	0.207 *	0.240 **
LVEF	0.094	0.038	0.056	-0.127	0.026
Heart Rate	-0.196*	-0.217*	-0.058	-0.168 +	-0.216 *
Sex	n.s.	n.s.	+	+	+
NYHA	+	n.s.	n.s.	n.s.	n.s.
Betablocker	n.s.	n.s.	n.s.	n.s.	n.s.
Major depression	***	***	***	***	***

*** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$.

LVEF, left ventricular ejection fraction; NYHA, New York Health Association.

Relation between changes in FEW16 values and clinical parameters and SF36

We further assessed whether the changes from baseline to FU2 measured by the FEW16 reflected the changes measured by the SF36 and PHQ-D and those of clinical parameters (Table 5). The FEW16 total score changes did not correlate with changes in 6MWT, LVEF, and heart rate, but they reflected the changes of the SF36 subscales *General Health Perceptions*, *Vitality*, *Social Functioning*, *Physical Functioning*, *Mental Health*, and the physical and the psychological components. Of the FEW16 subscales, *Vitality* correlated with SF36 *Physical Functioning*. *Inner Peace* was the FEW16 subscale that correlated with more SF36 scales (5 out of 10) than any other with two of those subscales relating to physical QoL (*Vitality* and *Role physical*). Resilience correlated with four out of nine SF36 subscales. With regard to depressive symptoms (PHQ-D), changes in the FEW16 total score had significant negative correlations with changes in *Little interest/pleasure in doing things*, *Feeling tired/having little energy*, *Difficulties sleeping*, *Physical impairments*, and *Thoughts of suicide*.

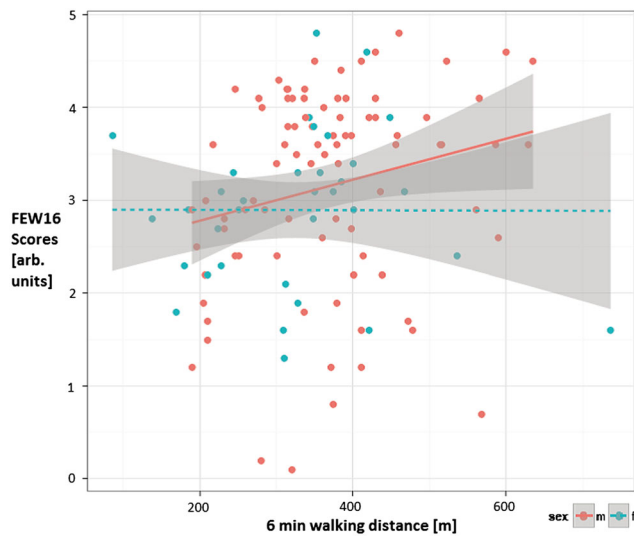
All FEW16 subscales but *Vitality* correlated with *Little interest/pleasure in doing things*, and all but *Ability to Enjoy* reflected the changes in *Feeling tired, having little energy*. All FEW16 subscales correlated significantly or had a strong tendency to correlate with *Thoughts of suicide*. *Inner Peace* was correlated with more PHQ-D subscales (six out of nine) than any other subscale.

Discussion

Validity of FEW16 for assessment of health-related Quality of Life

Aim of this study was the validation of the FEW16 as a disease-specific instrument for the assessment of physical well-being in HF patients. The FEW16 showed good reliability and internal consistency with high values for Guttman's lambda 6 and Cronbach's alpha, which were comparable to findings in previous validations.^{13,18}

Figure 3 Presumed gender specificity of the interdependence of the distance in the 6 min walking test and the FEW16 score. Base line FEW16 score over walking distance in the period of 6 min.



The factorial structure could be reconstructed with one exception, that item 8 appeared to have a slightly stronger association with subscale *Ability to Enjoy* than with *Resilience*. Given the high intercorrelation of subscales, all addressing the same generalized factor ‘well-being’, this deviation from the original factor score is not seen as critical problem potentially limiting the questionnaires use. In the original factor analysis defining the subscales,¹³ several items showed relevant factor loadings above 0.4 for more than one subscale and were assigned to the scale with the highest loading.

The FEW16 subscales showed significant correlations with all SF36 subscales. Subscales in the different questionnaires expected to measure constructs of the same content showed higher correlations than those measuring different constructs. For example, the finding that FEW16 *Vitality* correlated strongly with SF36 *Vitality*, and *Physical Functioning* confirmed that the FEW16 measured the correct construct in this place. *Vitality* is an important factor of physical well-being. This result confirms what Kolip & Schmidt found in their first validation study.¹³ The negative correlations of the FEW16 scores with those of the PHQ-D were expected as the PHQ-D measures the absence of well-being as opposed to the FEW16. The strong correlation of the FEW16 with depression underlines its validity, as depression is a common comorbidity in HF. In addition, Kolip & Schmidt differentiated between the QoL measured by the SF36 and physical well-being measured by the FEW16 as two different constructs, but agreed to a considerable overlap. For validation, they chose two SF36 subscales, *Vitality* and *Pain*, together with two questionnaires that assess back pain. Thus, they concentrated on the physical part of the FEW16. The fact that the FEW16 total score showed a stronger correlation with the

psychological than with the physical SF36 component does not contradict the FEW16’s validity, as it contains psychological questions as much as physical ones. Given the validity of the FEW16, this rather suggests a stronger impact of psychological factors on overall physical well-being than physical ones, in line with our results about the FEW16’s prognostic value. Faller *et al.*, examining the impact of depression and NYHA class on QoL, made the interesting conclusion: ‘in certain patients, Quality of life may depend to a larger extent on the presence and severity of depression rather than on the severity of heart failure’.¹¹ Taking this into account, the FEW16 seems to be a valid instrument to measure physical well-being in HF patients.

The FEW16, 36-Item Short-Form Health Survey, and PRIME MD Patient Health Questionnaire German short version questionnaires results

The SF36 results from this study confirm the SF36 results published in Scherer *et al.*,⁷ where all scores increased significantly during beta-blocker up-titration. All three questionnaires indicate an improvement of QoL and well-being from baseline to FU1, which was mostly annihilated at FU2. This pattern may result from the fact that beta-blocker up-titration happens at the beginning of the study so that changes in well-being and so on are most likely to occur at this stage. Later, patients may get used to their better health and may reflect less consistently on the difference between how they felt at baseline and FU2. Additionally, patients may experience a feeling of being taken care of and of hope for improvement of the illness at the beginning of the study, which, over time, may fade again, although this remains speculation until tested in more detail. An additional effect may result from the reduced number of patients at FU2.

Relation between clinical measurements and FEW16 scores

The negative correlations between heart rate and FEW16 total score and *Ability to Enjoy* and *Resilience* are interesting. Heart rate reduction is a therapeutic target of betablocker treatment of HF patients and lower heart rate correlated positively with lower mortality in elderly patients during the CIBIS-ELD trial. The achieved betablocker dose level on the other hand did not predict mortality.⁸ Our result that a lower heart rate was associated with better physical well-being seems to point into the same direction. The severity of HF expressed by LVEF and NYHA did not significantly correlate with any of the FEW16 scores, although we found a weak correlation between NYHA class and *Resilience*. This is consistent with the report by Müller-Tasch *et al.* that LVEF did not contribute to QoL.¹⁰ Some previous studies found that severity of

Table 5 Correlation coefficients between the changes of FEW16 values and changes of clinical and psychological parameters between baseline and FU2

Changes between base line and follow-up		Resilience	Ability to Enjoy	Vitality	Inner Peace	FEW16
Clinical	6 min walking distance	0.265	0.134	0.163	0.029	0.206
	LVEF	-0.153	0.135	0.032	-0.123	0.024
	Heart rate	0.029	0.157	0.009	0.085	0.097
SF36	Mental health	0.301*	0.462**	0.201	0.568***	0.457**
	Psychological, sum	0.401*	0.364*	0.177	0.612***	0.455**
	Vitality	0.519***	0.292	0.214	0.482***	0.453**
	Social functioning	0.288	0.301*	0.178	0.429**	0.425**
	Physical functioning	0.197	0.278	0.371*	0.219	0.420**
	Physical, sum	0.271	0.220	0.213	0.304	0.377*
	General health perceptions	0.374*	0.121	0.168	0.110	0.315*
	Role—emotional	0.291	0.141	0.080	0.311	0.227
	Role—physical	0.166	0.171	0.021	0.322*	0.224
	Pain	0.197	-0.075	0.184	0.054	0.108
PHQ-D	Little interest or pleasure in doing things	-0.427**	-0.384*	-0.211	-0.307*	-0.449**
	Feeling tired or having little energy	-0.393**	-0.267	-0.305*	-0.431**	-0.439**
	Difficulties sleeping	-0.136	-0.283	-0.528***	-0.180	-0.402**
	Physical impairments	-0.275	-0.413**	-0.138	-0.322*	-0.385*
	Thoughts of suicide	-0.292	-0.339*	-0.253	-0.398**	-0.338*
	Lack of self-confidence	-0.251	-0.288	-0.112	-0.394**	-0.297
	Poor appetite or overeating	-0.117	-0.212	-0.153	-0.173	-0.262
	Feeling down, depressed, hopeless	-0.213	-0.184	-0.133	-0.368*	-0.242
	Difficulties concentrating on things	-0.150	-0.157	-0.071	-0.213	-0.141

*** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$.

SF36, 36-Item Short-Form Health Survey; PHQ-D, PRIME MD Patient Health Questionnaire German short version; LVEF, left ventricular ejection fraction.

HF (i.e. NYHA class) predicts QoL,⁴⁰ in particular, the physical dimension of QoL.^{11,40} These differing results may be explained by the fact that Faller compared patients of NYHA class I/II with class III/IV, but 95% of our patients were in NYHA class II/III. Thus, the distribution of NYHA classes in our population may have been suboptimal to test for the impact of NYHA class on QoL. The FEW16 should be used on a larger and—regarding NYHA class—more heterogeneous sample to generate conclusive findings. The significant correlation of major depression with all FEW16 scores reflects the negative impact of depressed mood on the physical and psychological dimension of QoL in HF patients found earlier.^{10,11,40} Age and sex did not significantly correlate with any FEW16 score. We thus conclude, as did Kolip & Schmidt, that the FEW16 is gender-independent and age-independent. Nevertheless, our study did not show the positive correlation between male sex and *Inner Peace* that Kolip & Schmidt¹³ found in their first validation. Further, we did not find higher FEW16 total scores in men than women, as Albani *et al.*¹⁸ did in their non-clinical population. Both results may be explained by the difference in health status of the populations examined in the different studies. The 6MWT correlated significantly with *Resilience*, *Inner Peace*, and *Ability to Enjoy* in the whole patient sample. When examined in strata of gender, the FEW16 total score only correlated significantly with the 6MWT in men. This finding needs to be corroborated in a larger sample, but conclusions are intriguing: Are women more decisive in forcing their body to function? Do sexes differ in their perception of feeling physically well? Answers to these questions, some already

addressed in clinical studies,^{41–43} may contribute to improve the care of HF patients by applying better tailored strategies to their specific needs.

Relation between changes in FEW16 values and clinical parameters and SF36

Changes in the FEW16 correlated with the changes in both physical and psychological aspects of QoL between baseline and FU2, but not with changes in clinical parameters. Interestingly, although FEW16 *Vitality* showed a strong correlation with SF36 *Vitality and Physical Functioning* at baseline, its changes correlated not only with those in *Physical Functioning*, but also with those of PHQ-D subscales *Feeling tired/having little energy* and *Difficulties sleeping*. All FEW16 subscales but *Vitality* reflected the changes in *Little interest/pleasure in doing things* and all but *Ability to Enjoy* for those in *Feeling tired/having little energy*. Of particular importance, all FEW16 subscales had a tendency to or correlated significantly with *Thoughts of suicide*. Consistently, changes in *Inner Peace* correlated with changes of more PHQ-D subscales than any other. This underscores that the construct measured by the FEW16 in this trial was highly related to the QoL of our patients.

Impact of psychological vs. physical well-being

The FEW16 total score correlated stronger with the psychological than the physical SF36 component scale. This means

that the management team needs to be aware of the psychological and social situation of the patients in order to be able to best support patients' overall well-being. At the same time, it needs to be acknowledged that the interdependency between these factors requires more research.⁴⁴ Back in 1977, George L. Engel with his biopsychosocial model was first requesting to include a more holistic view of the patient into the definition and treatment of health and disease.⁴⁵ In 2004, Yolanda Alonso published a study where she investigated the frequency of inclusion of this concept into research papers and found no increase between the periods of 1978–82 and 1996–2000.⁴⁴ Our results once more strengthen the view that more factors impact on patient health than assessed through clinical measurements and that they should be included into treatment and research.

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Conflict of Interest

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