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ORIGINAL ARTICLE



The relationship between six-minute walked distance and health-related quality of life in patients with chronic heart failure

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ABSTRACT

Objectives. To assess the relationship between the six-minute walk test (6MWT) and health-related quality of life (HRQL) in patients with chronic heart failure. **Methods.** Forty-six patients (37 men and 9 women) with chronic heart failure, mean age 68 (SD 9), NYHA II–III and EF 29 (9) % were included. They performed 6MWT and assessed HRQL using two tools, a Swedish version of the 36-item Short Form (SF-36) and the Minnesota Living with Heart Failure Questionnaire (MLHFQ). This was performed repeatedly during a study period of one year. **Results.** Patients with a walking distance lower than median experienced a lower HRQL than the higher performing half of the cohort, in four dimensions of the SF-36 and the summary of physical and mental components, but not in the dimensions of MLHFQ. **Conclusion.** Patients with heart failure with a short walking distance assessed their quality of life as inferior in half of the dimensions in the SF-36 but not in the dimensions measured with the MLHFQ. Thus, different aspects of the symptomatology are uncovered using the 6MWT and the different HRQL tools.

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Introduction

Chronic heart failure (HF) has a significant impact on physical function and health-related quality of life (HRQL). The symptoms in HF, e.g. dyspnea and fatigue, may result in reduction of physical function and HRQL, which in turn affect activities of daily life [1–4]. Despite improvements in treatments, medical and non-medical, patients with HF often have persistent symptoms [4]. Although patient-assessed HRQL can predict mortality, cardiovascular events, hospital readmission and health care costs, this type of measurement is underutilized in clinical practice [5,6]. In clinical trials, however, it is common to use both generic and disease-specific questionnaires to evaluate patients' estimations of impact on quality of life [7]. Two questionnaires being frequently used in patients with HF, are the generic 36-item Short-Form Health Survey (SF-36) [8] and the disease-specific Minnesota Living with Heart Failure Questionnaire (MLHFQ) [9,10]. Alonso et al. [11] showed that patients with HF estimated the second lowest physical health by the SF-36 compared to patients with other chronic diseases.

The 6-minute walk test (6MWT) is a common and widely used test which represents and assesses physical function in patients with different conditions, and some studies

have shown that mortality, morbidity and hospitalization can be predicted based on the results of the 6MWT [12,13]. The simplicity of its implementation, performance, and interpretation makes it easy to use in clinical practice [12,13]. Guyatt et al. and the American Thoracic Society (ATS) [14,15] showed that, in patients with chronic obstructive pulmonary disease, the 6MWT can provide more information and a better index for measuring patient ability to perform daily activities, and correlates better with quality of life, than peak oxygen uptake. The walked distance of patients can be compared with reference data from the 6MWT performed in normal healthy populations [16,17].

The aim of the study was, by evaluating data from two prospective longitudinal training studies performed by our group, to explore the relationship between the 6-minute walked distance of the 6MWT and self-reported health-related quality of life evaluated with the dimensions and components of SF-36, and with MLHFQ, respectively, in patients with heart failure. We also hypothesized that rather than the absolute walking distance in meters at the 6MWT, would the walked distance in percent of the expected for each patient, be related to the quality of life estimates.

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Methods

Study population

This study utilizes data from two randomized longitudinal controlled trials (of which one, so far, has been published [18] with the primary objective of evaluating the results of exercise training interventions in heart failure with reduced ejection fraction [18]. Effects of different training regimes, home training or hospital based, were evaluated by the 6MWT, SF-36 and MLHFQ, using the same design for this evaluation in the two trials. Details about the training interventions have been published [18] and are not within the scope of this paper that is focused on the analysis of the instruments for evaluation of quality of life and physical performance, and the relation between them.

Patients were recruited from the outpatient cardiology clinic or hospital register on patients undergoing echocardiography at the department of clinical physiology, both clinics at Kalmar County Hospital, Sweden. Inclusion criteria in the main studies were left ventricular ejection fraction (EF) by echocardiography $\leq 40\%$, age ≤ 80 years, and the New York Heart Association's (NYHA) functional class II, or III. In addition, heart failure was to be stable with optimal

treatment of at least 3 months. Patient characteristics are presented in Table 1.

Exclusion criteria were concomitant chronic diseases, e.g. chronic obstructive pulmonary disease or diabetes, and physical or mental disorders that limited the ability to perform the 6MWT or complete the questionnaires.

The present study presents data from up to five follow-ups at three-month intervals. The test procedure was the same at all follow-up occasions.

The Regional Ethical Review Board of Linköping, Sweden approved the study (Dnr99266, Dnr02-041), and all included patients gave their written informed consent to participate. The investigation conforms to the principles outlined in the Declaration of Helsinki.

Evaluation of health-related quality of life

In order to evaluate HRQL validated Swedish versions of the SF-36 version 1 and MLHFQ were used. Both the SF-36 and the MLHFQ in Swedish have been tested for validity and reliability in a general Swedish population and in patients with heart failure [19,20]. The patients completed

Table 1. Patients characteristics at baseline.

Variable	6MWT			Total
	Pred < 92%	Pred \geq 92%	<i>p</i>	
<i>N</i>	24	22	46	
Age				
Mean (SD)	67 (8)	69 (10)	0,279	68 (9)
Gender				
Male	19 (79)	18 (82)	37 (80)	
Female	5 (21)	4 (18)	0,999	9 (20)
Weight (kg)				
Mean (SD)	85 (22)	81 (12)	0,506	83 (18)
Height (cm)				
Mean (SD)	176 (11)	172 (7)	0,117	174 (9)
BMI (kg m ⁻²)				
Mean (SD)	27 (6)	27 (3)	0,465	27 (5)
Number of tests/patient				
1-3	6 (25)	2 (9)	8 (17)	
5	18 (75)	20 (91)	–	38 (83)
EF (%)				
Mean (SD)	27 (8)	31 (9)	0,102	29 (9)
NYHA classification				
II	9 (38)	19 (86)	28 (61)	
III	15 (63)	3 (14)	<0.001	18 (39)
Cardiac medication				
ACE inhibitors	20 (83)	18 (82)	0.999	38 (83)
ARB	3 (13)	2 (9)	0.999	5 (11)
Diuretics	22 (92)	22 (100)	0.490	44 (96)
Betablockers	17 (71)	21 (95)	0.049	38 (83)
Diagnosis				
MI	17 (71)	11 (50)	28 (61)	
HT	2 (8)	0 (0)	2 (4)	
DCM	5 (21)	7 (32)	12 (26)	
AF	0 (0)	4 (18)	–	4 (9)
6MWT absolute distance (m)				
Mean (SD)	403 (77)	517 (67)	457 (92)	
Median (range)	401 (253–607)	527 (356–613)	–	438 (253–613)
6MWT % of predicted distance				
Mean (SD)	76 (13)	104 (10)	89 (18)	
Median (range)	77 (45–92)	104 (89–135)	–	89 (45–135)

Data calculated for those with a walked distance of less than median predicted (Pred <92%) and those more than Pred \geq 92%. Unless otherwise stated, numbers in brackets denote percentages. BMI: body mass index; EF: ejection fraction; NYHA: New York Heart Association Classification; ACE: angiotensin converting enzyme; ARB: angiotensin II receptor blockers; MI: myocardial infarction; HT: hypertension; DCM: dilated cardio myopathy; AF: atrial fibrillation; 6MWT: 6 min Walk Test.

the questionnaires at the same evaluation visit to the hospital as when the 6MWT was performed.

SF-36 is a self-reported instrument that evaluates generic HRQL, measuring overall health during the previous four weeks and comparing it to experienced health one year previously. The SF-36 is divided into eight subscales, which in turn can be grouped into two “summary measures” labeled the physical component summary (PCS) and mental component summary (MCS). The eight subscales are; Physical Functioning (PF), Role-Physical (RP), Bodily Pain (BP) and General Health (GH) forming the PCS and Vitality (VT), Social Functioning (SF), Role-Emotional (RE), Mental Health (MH), constituting the MCS. Response options are either YES/NO or graded in a Likert scale. The score goes from 0 to 100, where a higher score indicates better perceived health.

MLHFQ is a disease-specific measurement of HRQL estimating patients’ perceptions of the impact of heart failure on physical, emotional, and socioeconomic aspects of life [21,22]. MLHFQ contains 21 specific issues and measures patients’ experiences of how the HF has affected their health, including sleep, breathing, household chores and socializing during the last four weeks. The response is graded from 0=no to 5=very much (0–5), in a 6-point Likert scale. The scale’s range is 0–105 points, with lower scores indicating a better quality of life. Thus, questions reflecting a physical and an emotional dimension can be specifically evaluated. The physical dimension includes eight questions, 0–40 points. The emotional dimension includes five questions, 0–25 points. There was a later additional dimension, socioeconomic, not used in this study. Standardized instructions on how to inform participants were used [21,23].

Walk test

The 6MWT measures distance walked in 6 min. The walking test was performed in a flat, straight 80-meter course in an indoor hospital corridor. The length was marked every 2.5 meters and turnaround spots were marked with cones. The patients were instructed to walk as far as possible at their own pace, it was allowed to slow down, rest or stop and then continue to walk when able to [14,18]. Two 6MWT were performed on the same day with rest in a seated position for 45 min between walking tests with the intention to improve the accuracy of the test performance. No encouragement was given during the test. All patients were able to perform the test without any physical support. Heart rate was recorded with a heart rate monitor, (Polar®, Kempele, Finland) before and immediately after the 6MWT. Standardized oral instructions on how to use the Borg scales were given, and the patients were asked to rate their perceived exertion (RPE 6–20) and feelings of breathlessness (category ratio 0–10 (CR-10)) [24]. The result was the total walked distance covered in meters in six minutes. A stopwatch was used to record the time. All the 6MWTs were supervised by the same physiotherapist, not otherwise

involved in the studies, and who did not walk with the patients [14,25].

Data analysis and statistics

Data was analyzed by descriptive and inferential statistics and presented as the mean and standard deviation (SD). The outcome measure of the 6MWT was walked distance in meters, and the 6MWT with the longest walked distance, on each test occasion, was used in the analysis. Predicted walking distance in six minutes was calculated according to Enright’s formula [16]:

$$\text{Men} = (7.57 \times \text{height cm}) - (1.76 \times \text{weight kg}) - (5.02 \times \text{age}) - 309 \text{ m.}$$

$$\text{Women} = (2.11 \times \text{height cm}) - (2.29 \times \text{weight kg}) - (5.78 \times \text{age}) + 667 \text{ m.}$$

The percent of predicted walking distance was assessed from this data for each patient on every test occasion (baseline, 3, 6, 9 and 12 months). The median achieved walking distance, calculated for all tests performed, was 92% of the predicted value. Based on this, each patient on each test occasion was allocated to the dichotomized group with <92% or ≥92% of predicted, respectively, and simultaneously coupled to HRQL, measured with the two instruments SF-36 and MLHFQ. The analysis was then made using a mixed factorial ANOVA model with the various HRQL-scales (in total 8 + 2 summary SF-36 and 2 + 1 summary MLHFQ) as the dependent variables and, as independent categorical predictors, the dichotomized 6MWT (<92% or ≥92%), patient identification and test occasion. The interaction between the 6MWT (<92% or ≥92%) and test occasion allows statistically significant changes over time concerning the coupling between performance and HRQL to be estimated. The results are shown in Figures 1 and 2. Note that in Table 1, individuals were allocated to one of two groups (pred < 92% and pred ≥ 92%, respectively), according to the majority of the results of the five test occasions and are shown only for descriptive reasons. Statistical analysis was performed using Statistica version 12 (StatSoft®, Tulsa, OK, USA), and Excel 2013 (Microsoft Office, Redmond, WA, USA) and the significance level was set at $p < .05$.

Results

Baseline characteristics of the patients are presented in Table 1. A total of 46 patients with HF were evaluated (9 women aged 71 ± 7 years and 36 men aged 67 ± 9 years). EF was $29 \pm 9\%$ and 28 patients (61%) were in NYHA functional class II and 18 in NYHA class III (39%). In total, there were eight patients not fulfilling all five follow-ups over the year, for reasons unrelated to heart failure, e.g. lumbago, and relocation.

From a patient perspective, the mean walked distance at baseline was, for the group Pred < 92%, 403 ± 77 m (corresponding to $76 \pm 13\%$ of the predicted value) and, for the

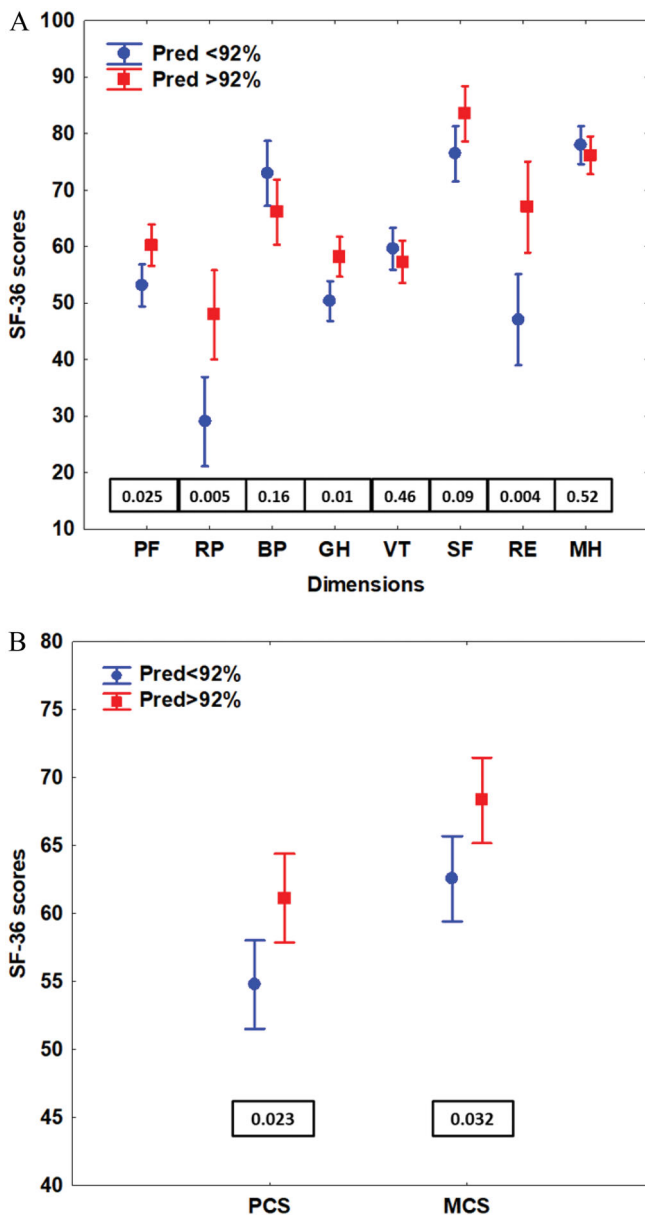


Figure 1. (A) Relationships between six-minutes walking distance and the 8 subscales of SF-36. Significant difference within each dimension indicates that a higher physical capacity (Pred $\geq 92\%$) is coupled to higher values of the SF-36-scaling, which indicates a higher HRQL. *p*-Values are presented on the bottom line. SF-36: short form 36 items; PF: physical functioning; RP: role-physical; BP: bodily pain; GH: general health; VT: vitality; SF: social functioning; RE: role-emotional; MH: mental health. (B) Corresponding relationships between six-minutes walking distance and the two summary components of SF-36. *p*-Values on the bottom line, for explanation see Figure 1(A). PCS: physical component summary; MCS: mental component summary.

group Pred $\geq 92\%$, 517 ± 67 m, corresponding to $104 \pm 10\%$ of the predicted value (Table 1).

There was a difference between the dichotomized walk test occasions, Pred $< 92\%$ and Pred $\geq 92\%$ regarding both the physical and mental component score measured with SF-36 (PCS and MCS) as well as 4 of the 8 subscales (PF, RP, GH, and RE; Figures 1(A,B)). The only interaction between performance and test occasion was found in RE, where the overall level ($p = .015$) in a following *post hoc* test shows a difference at baseline and 9 and 12 months, but not

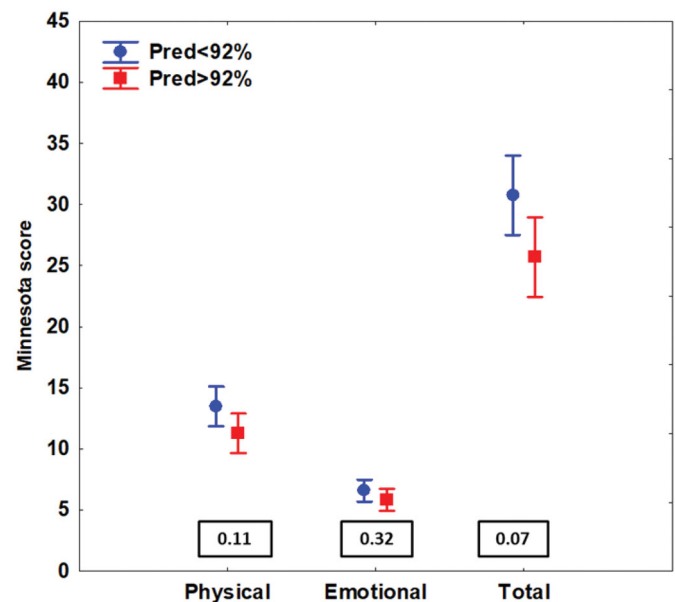


Figure 2. Relationships between six-minutes walking distance and the dimensions of the MLHFQ. *P*-values are presented on the bottom line, for explanation see Figure 1(A). Note that low values of these scales indicate a higher HRQL. MLHFQ: Minnesota Living with Heart Failure Questionnaire.

at 3 and 6 months. As regards MLHFQ no differences or interactions were found (Figure 2).

Discussion

To our knowledge this is the first study to evaluate the relationship between HRQL and the 6-minutes' walked distance, analyzed as % of the predicted for each individual, and at repeated test occasions over time, in patients with HF.

We chose to evaluate % of predicted walked distance rather than the absolute walked distance, as it takes gender, age, weight and height into account and was, therefore, hypothesized to better correspond to the patient's expectations and limitations.

The main findings of this study were that a higher 6MWT performance, i.e. belonging to the better half of our patient cohort with a walking distance above median, (Pred $\geq 92\%$) was associated with higher scores in the SF-36 for the PF, RP, GH, and RE dimensions, as well as the two component scores, PCS and MCS. No association was seen between walked distance and the dimensions of the disease-specific questionnaire, MLHFQ.

The difference in HRQL between groups with low and high performance at the 6MWT appeared to be more dominating in the physical dimensions of SF-36, than in the mental dimensions. This is in line with the study by Nogueira et al. [26] that examined the correlation between SF-36, MLHFQ, cardiopulmonary exercise test and 6MWT, in patients with HF. However, Nogueira et al. [26] performed the measurement on one occasion and used the absolute walked distance in the analysis, unlike our study where the relationship was evaluated up to five occasions and the % of predicted walked distance was used in the analysis. We judged this approach to be clinically relevant since repeated evaluations of HRQL and 6MWT will often take

place in longitudinal studies and that the performance at 6MWT related to the expected for each individual would characterize the degree of physical impairment more accurately than using the absolute walking distance.

No difference was seen regarding the disease-specific MLHFQ dimensions or the total score. Some studies have shown only a weak or nonexistent correlation between 6MWT and HRQL [27,28]. In the study by Nogueira et al. [26], the MLHFQ score showed a stronger correlation with the 6MWT than SF-36. Demers et al. [25] showed a significant, albeit weak, correlation between MLHFQ and 6MWT, all included patients walked less than 500 m. The results may be influenced by the degree of incapacitation and symptomatology of the patients studied. Studies have shown that medication, e.g. beta-blockers and ACE inhibitors, improves peak VO_2 and quality of life [29]. Conceivably, patients had already shown effects of the HRQL through medication, which may affect the relationship between physical function and HRQL.

In all studies on training in heart failure some patient selection would be inevitable e.g. the ability and willingness to participate may exclude the most symptomatic patients. We also excluded several comorbidities, which also would tend to select a better performing population, than the unselected heart failure population in clinical practice. On the other hand, this would make it possible to analyze the training effect with less confounders. Doherty et al. [30] showed that patients with HF and comorbidities, walked 42 m shorter than patients with less comorbidity. Among the inclusion criteria were being in NYHA class II or III. This might seem contradictory to the achieved walking distance of 92% of reference as a median value, but the NYHA classification is by its nature subjective, and takes other aspects than the pure physical ability to walk a certain distance into account. This study included patients with heart failure with reduced ejection fraction. Although patients with HF with preserved ejection fraction would also have been interesting to study, with the limited number of patients that was possible to train and evaluate simultaneously, we decided that this would not be possible within the framework of one study.

It is interesting to consider why several of the SF-36 dimensions were related to walking distance, but not the outcome of the MLHFQ evaluation. As our patients were stable on HF medication and not severely symptomatic, the MLHFQ might not uncover differences in aspects related to HF symptoms but the more general aspects on health related quality of life might still be related to physical performance. As a more general conclusion, it is valuable to carefully choose the instruments for effect evaluation since this will affect the possibility to detect results, and that it may be wise to use several different tests to reflect different aspects of performance and HRQL in heart failure.

Historically, HRQL and 6MWT have been labeled soft endpoints, unlike hard endpoints like morbidity and mortality. But Cooper et al. [31] state that there is growing evidence suggesting that these soft endpoints may be valuable in both research and clinical practice.

Heart failure affects physical function and HRQL negatively, particularly in the dimensions of general health and vitality [32,33]. Women with HF in particular seem to estimate poorer HRQL than men [1,34]. Other influencing factors that may affect quality of life are e.g. depression, younger age, higher body mass index and a larger symptom burden. Exercise can improve the HRQL but research findings vary [1,35]. In this study we have not taken any influencing factors into account, which would be of interest in future studies.

Limitation

A limitation of our study is the small number of participating women. However, it is well known that women are underrepresented in exercise studies for patients with HF [1]. Exclusion criteria were strict as no co-morbidity was allowed, and this may be considered a limitation and not representative of a mixed HF population. On the other hand, it sheds light on the performance of the questionnaires in relation to 6MWT without confounding comorbidity.

Conclusion

In a cohort of patients with stable heart failure in NYHA II or III, dichotomized according to performance at 6MWT in relation to predicted walked distance, patients with a high walked distance scored their quality of life according to the SF-36 higher in four specific dimensions, and the two (physical and mental) compound dimensions. However, there was no difference for the dimensions of the MLHFQ. It is concluded that the measurement of walking distance and evaluation of HRQL add complementary information, and that the different aspects of incapacity or symptoms in heart failure, depending on severity, may require different instruments for optimal evaluation, clinically and in research studies.

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