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Quality of life and survival in patients with heart failure

Tialda Hoekstra[1]*, Tiny Jaarsma[2], Dirk J. van Veldhuisen[1], Hans L. Hillege[1], Robbert Sanderman[3], and Ivonne Lesman-Leegte[4]

[1]Department of Cardiology, University Medical Center Groningen (UMCG), University of Groningen, PO Box 30.001, 9700 RB Groningen, The Netherlands; [2]Department of Social- and Welfare Studies, Department of Health Sciences, University of Linköping, Norrköping, Sweden; [3]Department of Health Sciences, University Medical Center Groningen (UMCG), University of Groningen, The Netherlands; and [4]Department of Epidemiology, University Medical Center Groningen (UMCG), University of Groningen, The Netherlands

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Aims To examine whether self-rated disease-specific and generic quality of life predicts long-term mortality, independent of brain natriuretic peptide (BNP) levels, and to explore factors related to low quality of life in a well-defined heart failure (HF) population.

Methods and results A cohort of 661 patients (62% male; age 71 years; left ventricular ejection fraction 34%) was followed prospectively for 3 years. Quality of life questionnaires (Ladder of Life, RAND36, and Minnesota Living with Heart Failure Questionnaire) and BNP levels were assessed at discharge after a hospital admission for HF. Three-year mortality was 42%. After adjustment for demographic variables, clinical variables, and BNP levels, poor quality of life scores predicted higher mortality; per 10 units on the physical functioning [hazard ratio (HR) 1.08, 95% confidence interval (CI) 1.02–1.14] and general health (HR 1.08, 95% CI 1.01–1.16) dimensions of the RAND36. Patients with low scores on these dimensions were more likely to be in New York Heart Association class III–IV, diagnosed with co-morbidities, have suffered longer from HF, have lower estimated glomerular filtration rates, and have fewer beta-blocker prescriptions.

Conclusion Quality of life was independently related to survival in a cohort of hospitalized patients with HF.

Trial registration: NCT 98675639.

Keywords Heart Failure • Quality of life • Survival • Mortality • Prognosis

Introduction

Heart failure (HF) has a negative impact on the length and quality of life (QoL) of patients.[1,2] Studies on whether QoL in itself has prognostic power for the prediction of mortality are inconsistent. Some, but not all, studies have found an association between poorer QoL and worse survival.[3] Inconsistencies in previous studies may be explained by their using different QoL instruments to predict outcomes. Most studies used one questionnaire, or focused on one subscale or question from a specific QoL questionnaire. Only a few have used disease-generic QoL questionnaires [Short Form-36 Health Survey (SF-36)] simultaneously with disease-specific QoL questionnaires [Minnesota Living with Heart Failure questionnaire (MLwHFQ), Kansas City Cardiomyopathy Questionnaire] in their patient population to describe the association between QoL and survival in HF patients.[3] Inconsistencies may also arise from the different follow-up periods used in the different studies, which ranged from a couple of months to > 5 years, and each study adjusted for different demographic and clinical variables.[4–8] The majority of studies did adjust for disease severity by using left ventricular ejection fraction (LVEF) or the New York Heart Association (NYHA) functional class.[3] However, both NYHA and LVEF have limitations as markers for disease severity. LVEF only reflects the severity of LV systolic dysfunction and not the severity of HF,[9] whereas NYHA classification is highly subjective based on the endurance of the patient and is directly associated with (physical) QoL. Furthermore, the utility of NYHA classification used as a marker of disease severity is currently the subject

* Corresponding author. Tel: +31 50 3610021, Fax: +31 50 3614391, Email: t.hoekstra@umcg.nl

of some debate owing to low inter-rater reliability.[10] Brain natriuretic peptide (BNP) has in recent years emerged as a reliable reflection of the severity of HF.[11] None of the aforementioned studies used BNP as a marker for the severity of HF.

Provided that QoL is a predictor of mortality, the important next step is to find out which patients have a low QoL. In order to reduce mortality, these patients in particular could benefit most from additional treatment, focused on improving QoL.

To gain more insight into the prognostic value of QoL, we examined the predictive value of several QoL instruments for long-term mortality in a large group of HF patients. In order to control with an objective parameter for the severity of HF, we adjusted for plasma levels of BNP in our analyses. Additionally, we examined the characteristics of patients with high and low QoL scores.

Methods

Patient population

Data were collected as part of the COACH study (Coordinating study evaluating Outcomes of Advising and Counselling in Heart failure). COACH was a multicentre, randomized clinical trial on the effect of a disease management programme in HF; the design, main results, and first QoL data have been published.[2,12–14] In brief, 1023 patients from 17 hospitals in The Netherlands were enrolled in the COACH study. Patients were included in the study during a hospitalization for HF (NYHA functional class II–IV), with HF as the primary diagnosis. The diagnosis was based on a combination of typical signs and symptoms according to the European Society of Cardiology (ESC) guidelines[15] for which a hospital stay was considered necessary. During hospitalization, all patients received standard care, both pharmacological and non-pharmacological, according to the guidelines,[15] in a cardiology ward, staffed by cardiologists and registered nurses. Patients were 18 years or older and had evidence of structural underlying heart disease. Exclusion criteria were: concurrent inclusion in a study requiring additional visits to research healthcare personnel; restrictions that made the patient unable to fill in data collection forms; an invasive intervention within the last 6 months or planned during the following 3 months; or ongoing evaluation for heart transplantation. All patients gave written informed consent.

The Central Ethics Committee approved the study protocol and the extended 3-year follow-up data collection on survival. The study was performed in accordance with the principles outlined in the Declaration of Helsinki.

Data collection

Plasma BNP levels were determined once and analysed locally within 4 h of blood collection (1 mL of blood, collected in EDTA), on the day of hospital discharge or on the day before hospital discharge. All BNP measurements were performed using a fluorescence immunoassay kit (Triage®; Biosite Incorporated, San Diego, CA, USA).[16] Data on LV function were obtained by standard transthoracic echocardiography.

Survival data were collected during the 18-month follow-up period of the COACH study as part of the primary endpoint of the study. Cause of death and the date of the event were adjudicated by a central endpoints committee. Concerning the patients who survived the 18-month follow-up period, 3-year follow-up (1095 days) data on all-cause mortality were collected from the hospital registry, and the general practitioner and/or municipality, 3 years after the last patients was included in the COACH study. For each patient who survived the initial 18-month follow-up, but died afterwards, a calculation was made on the time period between dying and inclusion in the COACH study in order to have an equally long follow-up period for each patient (1095 days).

Data on QoL were collected during hospitalization. Quality of life was assessed in three different ways: global well-being, disease-generic QoL, and disease-specific QoL.

Global well-being was assessed by Cantril's Ladder of Life. This is a single-item measure which asks the patient to rate their sense of well-being on a ladder, with 10 reflecting the best possible life imaginable and 0 reflecting the worst possible life imaginable. Cantril's Ladder of Life has been used in various cardiovascular studies and is considered to be a valid measure of global well-being.[17] A higher score indicates better well-being.[18]

Disease-generic QoL was assessed by the Medical Outcome Study 36-item General Health Survey (RAND36), a self-report questionnaire of general health status and comparable with the SF-36.[19,20] The RAND36 is a well-validated generic, 36-item questionnaire that includes nine health concepts that represent dimensions of QoL: physical functioning, social functioning, role limitations because of physical functioning, role limitations because of emotional functioning, mental health, vitality, bodily pain, general health, and perceived health change. Each dimension has a score between 0 and 100; a higher score means better health.[19]

Disease-specific QoL was measured with the MLwHFQ.[21] The MLwHFQ is a 21-item scale, with a scoring range of zero for no impairment, to 105 for maximum impairment as a result of HF. Three scores can be determined: a total score (21 items, 0–105), the physical dimension (8 items, 0–40), and the emotional dimension (5 items, 0–25). Higher scores mean a worse QoL. The questions cover symptoms and signs relevant to HF, e.g. physical activity, social interaction, sexual activity, work, and emotions. All patients were instructed by trained data collectors to report if, and to what extent, HF has affected their life during the last month on each item. The reliability and validity of the MLwHFQ have been documented.[21]

Statistical analysis

Descriptive statistics were used to characterize the study population. Data are presented as means ± standard deviations (SDs) or percentagess. Student's *t*-tests and Mann–Whitney tests for continuous variables, and χ^2 tests for categorical variables were performed to compare demographic characteristics, clinical characteristics, and QoL between patients who survived and did not survive the 3-year follow-up period. Cox proportional hazards regression was used to determine the independent association of QoL with time to mortality. Separate analyses were made for each scale: the nine dimensions of the RAND36, both subscales and total score of the MLwHFQ, and the Ladder of Life. To evaluate a possible effect-modifying role of potential risk factors with regard to mortality, three Cox regression analyses were performed: first including the QoL scale, secondly adjusting for age and gender, and finally adjusting for all variables with a theoretical or univariate association with mortality (*P*-value <0.10 two tailed). Within the third model there was no hierarchical inclusion of the variables. All variables were entered as dummies, except for age, BNP, QoL scales, systolic blood pressure, diastolic blood pressure, heart rate, sodium, and estimated glomerular filtration rate (eGFR), which were modelled as continuous variables. The RAND36 dimensions and the total score of the MLwHFQ were recoded per 10 units. To gain hazard ratios (HRs) >1.00 for reasons of readability, the scores of the RAND36 dimensions per 10 units and the Ladder of Life

scores were subtracted from 10. All QoL scales were stratified by centre.

More in-depth analyses on patient characteristics of the two QoL dimensions with the highest prediction on survival were performed. We compared patients who scored in the lowest quartiles with patients who scored in the highest quartiles on these dimensions. Kaplan–Meier curves with a log-rank test were constructed for the patients in the lowest and highest quartiles of both dimensions.

Statistical significance was set at two-tailed $P < 0.05$. Analyses were performed with STATA version 11 (StataCorp., College Station, TX, USA).

Results

Patient characteristics

Of the 1023 patients included in the main COACH study, a BNP level was available in 766 patients. Within the patient sample of 766 patients, all QoL questionnaires at baseline were completed by 661 patients (86%). Only patients with available BNP levels who completed all questionnaires were included in the current study. Patients who were excluded from the current study did not differ from the study sample on age, gender, NYHA functional class at discharge, and LVEF function.

Patients had a mean age of 71 years (± 11), 61% was male, and 40% were living alone. The mean LVEF was 34% (± 14), 33% had an LVEF >40%, and at discharge 51% were classified as NYHA functional class III–IV (*Table 1*). During the 3-year follow-up, 276 (42%) patients died; no patients were lost to follow-up. Patients who died during the follow-up period were significantly older, more often in NYHA III–IV, had higher BNP levels at hospital discharge, lower systolic and diastolic blood pressure, lower eGFRs, had been diagnosed with HF for longer, were more often previously hospitalized for HF, and were more often diagnosed with diabetes or had a stroke in the past than patients who survived the 3-year follow-up period. Furthermore, the survivors were more often treated with angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs) and beta-blockers at discharge than the non-survivors (*Table 1*).

Table 1 Baseline characteristics according to mortality

	Total group ($n = 661$)	Survivors ($n = 385$)	Non-survivors ($n = 276$)	*P*-value[a]
Demographics				
Age (years)	71 ± 11	68 ± 12	74 ± 10	<0.001
Male	62%	58%	64%	0.147
Living alone	40%	39%	42%	0.336
Smoking	17%	18%	15%	0.290
Clinical characteristics				
LVEF %	34 ± 14	34 ± 14	34 ± 14	0.916
NYHA III–IV	51%	45%	59%	<0.001
Systolic blood pressure (mmHg)	118 ± 21	120 ± 21	116 ± 20	0.039
Diastolic blood pressure (mmHg)	69 ± 12	70 ± 12	66 ± 12	<0.001
Heart rate (b.p.m.)	75 ± 13	75 ± 14	74 ± 12	0.409
BNP (pg/mL) median (IQR)	447 (202–869)	342 (161–725)	572 (300–1110)	<0.001
Sodium (mEq/L)	139 ± 4.7	139 ± 4.6	138 ± 4.9	0.186
eGFR (mL/min/1.73 m^2)	57 ± 22	61 ± 22	50 ± 20	<0.001
Hypertension	44%	44%	43%	0.968
Ischaemic heart failure	42%	38%	46%	0.041
Duration of heart failure (years)	2.7 ± 4.5	2.0 ± 3.8	3.7 ± 5.1	<0.001
> 1 previous heart failure hospitalization	33%	26%	43%	<0.001
Medication				
ACE inhibitors/ARB	84%	87%	81%	0.030
Beta-blockers	65%	68%	61%	0.043
Diuretics	97%	96%	98%	0.121
Co-morbidities				
COPD	27%	25%	29%	0.180
Diabetes	28%	23%	34%	0.001
Stroke	9%	7%	12%	0.029
Renal disease	7%	7%	8%	0.444

[a]Comparison between survivors and non-survivors.

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BNP, brain natriuretic peptide; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association functional class.

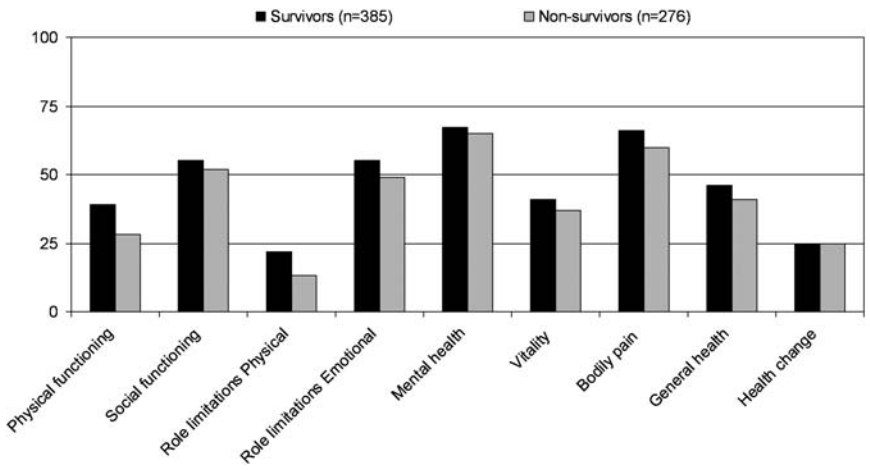

Figure 1 Quality of life as measured by the RAND36 at baseline according to mortality.

Quality of life

Global well-being at baseline, as measured with Cantril's Ladder of Life, did not differ significantly between survivors and non-survivors (6.3 ± 1.7 vs. 6.2 ± 1.9, $P = 0.170$).

Mean scores of all dimensions of the RAND36 in the total group varied between 18 and 66 on the theoretical range between 0 and 100, with the lowest scores for role limitations physical (18 ± 33), health change (25 ± 23), and physical functioning (34 ± 26). Non-survivors had a significantly lower QoL at baseline than survivors on the physical functioning (28 ± 23 vs. 39 ± 27, $P < 0.001$), role limitations physical (13 ± 27 vs. 22 ± 36, $P < 0.001$), bodily pain (60 ± 34 vs. 66 ± 34, $P = 0.031$), and general health (41 ± 18 vs. 46 ± 19, $P = 0.001$) dimensions (*Figure 1*).

The mean score in the total group on the total scale of the MLwHFQ was 44 ± 21. On the physical and emotional subscales, mean scores were 24 ± 23 and 7.1 ± 6.1, respectively. On the MLwHFQ, non-survivors rated their QoL at baseline significantly lower than survivors on the total score (47 ± 19 vs. 42 ± 22, $P = 0.010$) and the physical subscale (25 ± 9 vs. 22 ± 11, $P = 0.001$). The emotional subscale scores of the MLwHFQ at baseline did not differ between survivors and non-survivors (6.9 ± 6.1 vs. 7.3 ± 6.1, $P = 0.380$).

Survival analyses

Univariate analyses (model 1) show a HR of 1.15 (95% confidence interval1.09–1.21) per 10 units on the physical functioning dimension of the RAND36, which indicates an increase of 15% in mortality per 10 units decrease on the physical functioning score. Furthermore, a decrease in scores per 10 units on the role limitations physical, bodily pain, and general health dimensions of the RAND36 showed a significant increase in mortality (8, 4, and 12%, respectively). An increase in score per 10 units on the total score of the MLwHFQ and per one unit on the physical functioning score of the MLwHFQ also showed a significant increase of 7% and 2% in mortality (*Table 2*).

After adjusting the model for age, gender, NYHA, smoking, systolic blood pressure, diastolic blood pressure, heart rate, BNP level, sodium level, eGFR, ischaemic HF, duration of disease, previously hospitalized for heart failure more than once, ACE inhibitors/ARBs, beta-blockers, diuretics, diabetes, stroke, and renal disease (model 3), the physical functioning and general health dimensions of the RAND36 were associated with mortality (*Table 2*).

Patient characteristics related to low physical functioning and general health

Patient characteristics were compared between patients who scored in the lowest quartile of physical functioning (range 0–15) and general health (range 0–30) and the highest quartile (ranges 50–100 and 55–100, respectively). Patients with a low QoL on physical functioning were older, more often female, more often in NYHA III–IV, had higher BNP levels at discharge, lower sodium levels, lower diastolic blood pressure, lower eGFRs, were more often diagnosed with chronic obstructive pulmonary disease (COPD), diabetes, and stroke, had a longer duration of HF, were more often previously hospitalized for HF, and less often had a prescription of beta-blockers at discharge, than patients with high physical functioning (*Table 3*).

Patients with a low QoL on the general health dimension were also more often in NYHA III–IV, diagnosed with COPD and stroke, had suffered longer from HF, were more often previously hospitalized for HF, had lower eGFRs, and were more often diagnosed with renal disease than patients with a high QoL on the general health dimension (*Table 3*).

During the 3-year follow-up period, 84 of the 157 patients (54%) with a low physical functioning score, and 39 of the 151 patients (26%) with a high physical functioning score, died ($P < 0.001$, *Figure 2*). Of the 133 patients with a low general health score, 75 patients (56%) died, compared with 54 of the 153 patients (35%) with a high general health score ($P < 0.001$, *Figure 3*).

Table 2 Cox proportional hazards regression of the quality of life subscales on time to mortality ($n = 661$)

	Model 1		Model 2		Model 3	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Ladder of Life[a]						
Well-being	1.04 (0.98–1.11)	0.222	1.05 (0.98–1.12)	0.148	1.01 (0.94–1.08)	0.738
RAND36 (per 10 units)[a]						
Physical functioning	1.15 (1.09–1.21)	<0.001	1.13 (1.07–1.20)	<0.001	1.08 (1.02–1.14)	0.008
Social functioning	1.01 (0.97–1.05)	0.576	1.02 (0.99–1.06)	0.343	0.98 (0.95–1.02)	0.438
Role limitations—physical	1.08 (1.03–1.13)	0.001	1.08 (1.04–1.13)	<0.001	1.04 (0.99–1.08)	0.128
Role limitations—emotional	1.02 (1.00–1.05)	0.055	1.02 (1.00–1.05)	0.071	1.01 (0.98–1.04)	0.559
Mental health	1.03 (0.98–1.08)	0.289	1.06 (1.00–1.11)	0.032	1.04 (0.99–1.10)	0.150
Vitality	1.05 (1.00–1.11)	0.053	1.07 (1.02–1.13)	0.007	1.03 (0.98–1.09)	0.256
Bodily pain	1.04 (1.00–1.08)	0.029	1.04 (1.00–1.07)	0.044	1.03 (0.99–1.07)	0.109
General health	1.12 (1.05–1.20)	0.001	1.13 (1.06–1.21)	<0.001	1.08 (1.01–1.16)	0.032
Health change	1.01 (0.96–1.06)	0.681	1.02 (0.96–1.07)	0.557	1.00 (0.95–1.05)	0.923
Minnesota Living with Heart Failure Quesionnaire[b]						
Total (per 10 units)	1.07 (1.02–1.13)	0.012	1.12 (1.06–1.19)	<0.001	1.05 (0.98–1.12)	0.172
Physical functioning	1.02 (1.01–1.03)	0.002	1.02 (1.01–1.03)	<0.001	1.01 (0.99–1.02)	0.350
Emotional functioning	1.01 (0.99–1.03)	0.302	1.03 (1.01–1.05)	0.012	1.01 (0.99–1.03)	0.304

Model 1: no adjustments
Model 2: adjustment for age and gender
Model 3: adjustment for age, gender, smoking, New York Heart Associtiation, systolic blood pressure, diastolic blood pressure, heart rate, brain natriuretic peptide level, sodium level, estimated glomerular filtration rate, ischaemic heart failure, duration of disease, previously hospitalized for heart failure more than once, angiotensin-converting enzyme inhibitors/angiotensin receptor blocker, beta-blockers, diuretics, diabetes, stroke, and renal disease.
CI, confidence interval; HR, hazard ratio.
[a]A higher score means better health.
[b]A higher score means worse health.

Discussion

The main finding of the present study is that QoL independently of BNP values predicts 3-year mortality in patients with HF. To our knowledge this is the first study in a large and clinically relevant group of HF patients in which the effect of QoL on mortality is adjusted for BNP levels, a widely accepted marker for disease severity and a prognostic tool to predict mortality.[11,22]

Previous research showed inconsistent results on physical QoL to be a predictor of mortality.[3] When looking at the four studies which used a disease-specific QoL questionnaire and had a follow-up period > 2 years, all studies found a significant association between the physical component of their questionnaire and mortality.[6,7,23,24] However, our results on the physical dimension of the MLwHFQ being a predictor for survival independent of BNP levels do not confirm these findings. Studies including the physical dimensions of disease-generic QoL questionnaires to predict mortality are not consistent.[6,7,25,26] Two studies did find physical functioning to be independently associated with mortality,[7,25] and two other studies did not find this association.[6,24] However, these two studies had limitations in the generalizability of their results due to their relatively small sample size[26] and a very specific HF patient sample, namely male veterans.[6] Both studies which showed consistent findings had a relatively large ($n = 3375$ and $n = 433$) and a more generalizable HF patient sample.[7,25]

In our study we extend previous studies by taking the research to the next level by exploring which patients report low QoL in order to address future interventions for improving QoL, and reducing mortality. In our data we found several factors related to low QoL that could be used in identifying patients with low QoL, e.g. higher age, female gender, being diagnosed with HF for longer, and co-morbidities. Other factors related to low QoL which can be used to identify patients, but which also can be influenced by interventions and therefore possibly improve QoL, are high NYHA functional class (III–IV), low eGFRs, and no prescription of beta-blockers.

To improve NYHA functional class, it can be suggested to include an exercise component in the treatment programmes of HF patients. Several studies have shown that exercise programmes improve QoL.[27] Two meta-analyses of exercise-based rehabilitation clinical trials in patients with HF identified a significant benefit of exercise training on all-cause mortality and total cardiac mortality.[28,29] Furthermore, our results show that patients with a low QoL had fewer beta-blocker prescriptions. The effectiveness of beta-blockers for mortality is well tested,[1] and showed a trend towards improvement of QoL in patients receiving beta-blocker therapy.[30]

The current study underlines the importance of QoL in patients with HF.[31] Previous research on patients' preferences show that patients give equal or more importance to QoL when compared

Table 3 Patient characteristics; low vs. high quality of life

	Low physical functioning ($n = 157$)	High physical functioning ($n = 151$)	*P*-value	Low general health ($n = 133$)	High general health ($n = 153$)	*P*-value
Demographics						
Age (years)	74 ± 10	67 ± 11	<0.001	70 ± 12	72 ± 11	0.301
Male	47%	72%	<0.001	56%	59%	0.678
Living alone	46%	36%	0.079	39%	46%	0.256
Smoking	16%	19%	0.433	12%	18%	0.177
Clinical characteristics						
LVEF %	34 ± 15	32 ± 14	0.219	35 ± 15	35 ± 15	0.975
NYHA III–IV	69%	26%	<0.001	66%	33%	<0.001
Systolic blood pressure (mmHg)	117 ± 22	121 ± 21	0.109	115 ± 21	120 ± 21	0.055
Diastolic blood pressure (mmHg)	67 ± 13	71 ± 12	0.007	68 ± 13	70 ± 12	0.103
Heart rate (b.p.m.)	75 ± 13	74 ± 14	0.474	74 ± 14	73 ± 13	0.536
BNP (pg/mL) median (IQR)	497 (244–1090)	348 (162–747)	0.017	502 (232–1070)	389 (179–801)	0.125
Sodium (mEq/L)	137 ± 5.9	139 ± 4.3	<0.001	138 ± 5.3	139 ± 5.2	0.087
eGFR (mL/min/1.73 m^2)	51 ± 19	62 ± 21	<0.001	52 ± 22	58 ± 19	0.021
Hypertension	47%	42%	0.399	44%	39%	0.452
Ischaemic heart failure	39%	40%	0.874	39%	42%	0.561
Duration of heart failure (years)	3.6 ± 5.1	1.4 ± 2.8	<0.001	3.8 ± 5.5	1.6 ± 3.6	<0.001
> 1 previous heart failure hospitalization	47%	24%	<0.001	47%	22%	<0.001
Medication						
ACE inhibitors/ARB	82%	89%	0.076	84%	86%	0.739
Beta-blockers	58%	73%	0.006	64%	67%	0.625
Diuretics	97%	95%	0.511	97%	97%	0.900
Co-morbidities						
COPD	33%	14%	<0.001	35%	12%	<0.001
Diabetes	39%	21%	<0.001	25%	20%	0.290
Stroke	13%	5%	0.023	16%	4%	0.001
Renal disease	7%	6%	0.710	11%	3%	0.008
Quality of life						
Physical functioning[a]	6 ± 4	74 ± 15	<0.001	21 ± 19	50 ± 29	<0.001
General health[a]	36 ± 17	55 ± 18	<0.001	19 ± 7	70 ± 9	<0.001

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BNP, brain natriuretic peptide; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association functional class.
[a]A higher score means better health.

with length, and about half of a HF patient population is willing to select therapies that improve their QoL, even if this leads to shortening of life,[32,33] although one study showed the opposite results.[34] In the past, study outcomes focused mainly on reducing hospitalizations and mortality. Nowadays, QoL is increasingly incorporated as an outcome measure in clinical trials.[35–37] Furthermore, in the HF guidelines, improving QoL is recognized as one of the major treatment goals.[15] Adding our findings that QoL is independently associated with mortality, to the relevance of QoL for individual patients, for research outcomes, and for clinical practice, the value of QoL cannot be ignored. It is of great importance to develop and evaluate treatment programmes that effectively improve QoL in HF patients. However, there are few randomized studies that specifically focus on improving QoL in patients with HF. Some studies on disease management programmes have shown improvement in QoL as a result; unfortunately, the findings are inconsistent.[38]

It might be debated that the concepts QoL and depression are overlapping. Quality of life is defined by the World Health Organization as 'an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns'.[39] Depression is defined by the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) as a mental disorder that presents with depressed mood, loss of interest or pleasure, weight loss, feelings of guilt or low self-worth, disturbed sleep or appetite, fatigue and poor concentration, and can be classified under the heading of the psychological function of the QoL domains.[40] From our COACH database, we previously published data that showed that 39% of patients with HF had depressive

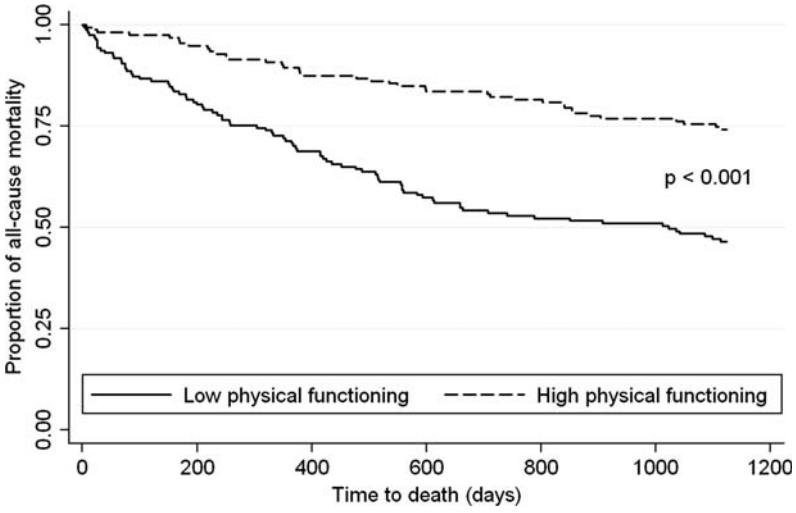

Figure 2 Kaplan–Meier curves for time to death in patients with low physical functioning and high physical functioning.

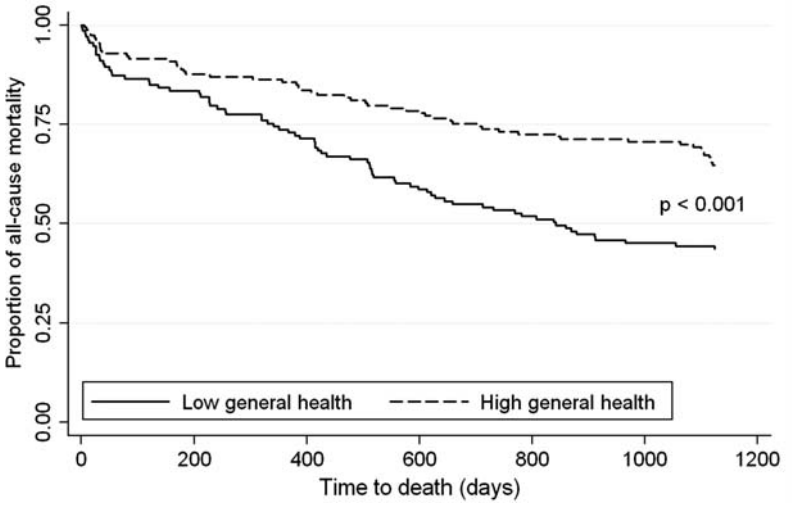

Figure 3 Kaplan–Meier curves for time to death in patients with low general health and high general health.

symptoms [Center for Epidemiological Studies Depression scale (CES-D) score $\geq$16], and having severe depressive symptoms was significantly associated with death and readmission within 18 months of follow-up after a hospital admission.[41] In the current study we did not include depressive symptoms measured by the CES-D, but did include several mental health and emotional dimensions of the different QoL questionnaires. These dimensions include fewer items than the CES-D, and are not specifically focused on depression, but more on emotions and mental health in general.

The present study is limited, in that the follow-up period for mortality was 3 years, which is relatively short compared with other studies on QoL being a predictor for long-term mortality which have used follow-up periods of 5– 7 years.[6,7] However, our sample size was relatively large ($n = 661$) compared with the previous studies on long-term mortality, which had sample sizes of 459 and 416 HF patients, respectively. Furthermore, our mortality rate was 42%, which is comparable with the mortality rates of both the other long-term follow-up studies (e.g. 44% and 70%) and therefore high enough for reliable analyses on comparing QoL between survivors and non-survivors. A second limitation is generalizability of the study cohort. Only hospitalized patients with HF were included, which is only a part of the total HF patient population.

In conclusion, the present study is the first study on QoL and long-term mortality in HF in which BNP levels were used as an

objective marker to reflect the severity of HF. Our results show that QoL assessed during a hospitalization for HF is a predictor for 3-year mortality independent of BNP levels and a wide range of demographical and clinical variables. In particular, general health and physical functioning assessed with a disease-generic QoL questionnaire provide prognostic information on survival in addition to other prognostic variables. Patients with low scores on these dimensions were more likely to be in NYHA III–IV, diagnosed with co-morbidities, suffered from HF for longer, had lower eGFRs, and had fewer beta-blocker prescriptions.

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