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Exploring quality of life in patients with and without heart failure

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ABSTRACT

Aims: The EuroHeart Failure Survey Questionnaire (EHFSQ-1) has 39 questions on symptoms and quality of life (QoL); many items are related. We sought to identify underlying clusters amongst EHFSQ-1 questions, construct an overall "QoL score" and investigate its relationship to a single question asking patients to self-rate QoL.
Methods and results: Factor analysis based on the principal component technique was used to identify patterns amongst responses to QoL questions from patients referred with symptoms suggesting heart failure (HF). Of 1031 patients, median age 71 (IQR: 63–77) years, 64% were men and 626 had confirmed HF. For patients with HF, seven symptom-clusters were identified: "breathlessness", "psychological distress", "sleep quality", "frailty", "cognitive/psychomotor function", "cough" and "chest pain". These clusters accounted for 65% of the total variance in QoL score. Cluster pattern was similar in patients with and without HF. A summary factor score was tightly correlated with summary QoL score (correlation coefficient: $r = 0.96$; $p < 0.0001$). Both summary factors and QoL scores were highly correlated with patient self-rating of overall health ($r_1 = 0.61$ and $r_2 = 0.66$ respectively, $p < 0.0001$) or overall QoL ($r_1 = 0.60$ and $r_2 = 0.66$, $p < 0.0001$). The medians (IQR) of the summary QoL score for patients with HFrEF, HFnEF and no-HF were, respectively, 83 (60–106), 82 (59–104) and 71 (51–94).
Conclusions: EHFSQ-1, comprises seven symptom clusters in patients with HF. Either summary factors or QoL scores can be used as a QoL outcome measure. However, if the key question is 'what is this patient's QoL?' rather than the reason why it is impaired, then a single, direct question may suffice.

1. Introduction

The goals of treating heart failure are to maintain or improve the quality of life by managing symptoms and reducing morbidity and disability and to prolong useful life. Ultimately, improving the 'patient journey' [1] or quality-adjusted life-years is the objective of both patients and their doctors. However, most clinical trials of heart failure focus on morbidity and mortality rather than on quality of life (QoL), which is usually measured infrequently during the course of the trial, if at all. This partly reflects a lack of confidence amongst both trialists and regulators about the validity of tools used to assess QoL and partly the perceived burden on both patients and investigators of completing existing QoL questionnaires repetitively. However, QoL questionnaires are asking two distinct questions; firstly "what is this patient's QoL?" and secondly, "if impaired, 'why'?". However, in a clinical trial the first question may be of greater importance. The second may give insights into how an intervention has changed QoL but with few exceptions [2], this is never reported in trials. This issue could be addressed if investigators and regulators were willing to accept that the patient is the best judge of their QoL which could reduce the complexity of assessment of QoL to a single question that could be asked at every visit. This would permit the calculation of average QoL throughout the study as well as an assessment of the impact of morbid events on QoL. Trying to measure QoL using questionnaires is not straightforward. Inevitably, questionnaires concentrate on symptoms thought to be important by clinicians, but not necessarily patients, and include a large number of questions that are often highly related. Factor analysis (FA) [3,4] reduces complex information by identifying latent structures in the data and extracting highly correlated sets of symptoms as "symptom clusters". Each symptom cluster can be scored and used for further analysis [5,6].

The aim of the present study was to identify symptom clusters in the EuroHeart Failure Survey Questionnaire used in the first survey (EHFSQ-1), to construct an overall "QoL score" from them and then to relate this score to patient self-reported QoL using single questions [7,8] using data acquired routinely as part of a clinical heart failure service.

2. Methods

Patients referred to a community heart failure clinic (Kingston-upon-Hull, UK) for the assessment of heart failure symptoms were invited to participate. Patients underwent clinical examination, including demographic measurements, symptoms and signs,

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electrocardiograms, echocardiography and routine haematology and biochemical investigations. The questionnaire was designed by a group of experts to obtain data on symptom severity and quality of life in the first EuroHeart Failure survey. It has not, as far as we are aware, been subjected to detailed methodological validation.

Patients were sent the EuroHeart Failure Survey Questionnaire (EHFSQ-1), which comprises 39 questions (Tables 2.1 and 2.2), in the post prior to attending the clinic. No restriction was placed on seeking the advice and opinion of friends and relatives. The first 37 questions (1–37) ask about specific symptoms. The response to each question could be: no, very little, a little, some, a lot, very much, unknown and was coded from 1 to 6; unknown was coded as 7 and was excluded in this study. The following four questions (18–21) were very often left unanswered: inability to work due to your health; side effects that you think might be due to your treatment; difficulties with sexual function; and cost of medicines or medical care. They were excluded for the purposes of this analysis. The final two questions (38–39) ask about general health, and overall quality of life. Each could be answered: very good, good, quite good, average, quite poor, poor, very poor and unknown. The responses to both questions were coded from 1 to 7; unknown was coded as 8 and was excluded in the study.

All patients provided written informed consent for their data to be used and the study was carried out in accordance with the Helsinki Declaration II and the European Standards for Good Clinical Practice. Ethical approval was granted by the Hull and East Yorkshire Local Research Ethics Committee.

Patients were enrolled at first assessment in an out-patient clinic and all had a history suspicious of heart failure or concerns about important cardiac dysfunction. In the context of the sort of patients referred, heart failure was defined as being present if the left ventricular ejection fraction (LVEF) was less than 40% (heart failure with reduced ejection fraction; HFrEF) or, if LVEF was ≥40%, by an NT-proBNP > 400 ng/L (heart failure with normal ejection fraction; HFnEF). Patients who had both LVEF > 40% and NT-proBNP < 400 ng/L were considered not to have heart failure for the purposes of this analysis, although other thresholds and criteria were considered.

2.1. Statistical analysis

Continuous variables are expressed as a median with inter quartile range; and categorical variables are given as percentages. Differences between the groups were examined using independent t-test or Mann–Whitney U test and chi-square tests for continuous and categorical variables respectively. Pearsons correlation coefficient and Spearmans correlation coefficient with scatter plots were used to assess the correlations or relationships between two variables depending on the distribution of the data.

Exploratory factor analysis (FA) was performed using principal component analysis (PCA). PCA is a data reduction technique which transforms a number of correlated variables into a smaller number of uncorrelated variables termed principal components (that is, linear combinations of the original variables) which explain a large proportion of the original sample variance. The 4 questions 18–21 mentioned above were not included in the analysis due to too many missing values and general overall QoL and overall health were not included. The remaining 33 questions were considered in the analysis.

To identify QoL symptom clusters, only principal components with initial eigenvalues >1 were extracted and an orthogonal factor rotation with Varimax method [9] applied. The symptom clusters were labelled according to the characteristics of the original variables. Variables with a factor loading >0.4 were considered to be an important component of an underlying symptom cluster (Factor loading is a correlation between a variable and a factor. The higher the load the more relevant in defining the factor.). Symptom cluster scores were calculated based on the Anderson–Rubin method [10] for further analysis. The sampling adequacy was checked by the Kaiser–Meyer–Olkin (KMO) test [11]. The 10-fold cross-validation was used to assess the stability of the analysis and Cronbach's alpha [12] was used for testing the reliability of questions on each symptom cluster.

Overall QoL scores were derived using either (1) the raw summary scores (ranging potentially from 31 (very good health) to 186 (terrible health)); or (2) the summary factor scores derived by the sum of each symptom cluster score, ranging from −5 to 10 in this dataset (a big number is associated with a bad health).

Statistical analysis was carried out using SPSS 17 software package. The two-tailed level of statistical significance was set at $p < 0.05$.

3. Results

3.1. Baseline characteristics

Of 1031 patients, 657 (64%) were men and the median age was 71 years (IQR: 63–77), 626 had HF (377 with HFrEF and 249 with HFnEF) and 405 did not fulfil the criteria for HF (Table 1). As expected, patients with HF had more severe symptoms, more cardiovascular problems, poorer renal function and substantially higher plasma concentrations of NT-proBNP despite receiving more loop diuretics, ACE inhibitors, beta blockers and spironolactone. Patients with HFnEF were older, more often women and had more atrial fibrillation and diabetes. BMI was greater in patients without heart failure but the rate of reported COPD was similar in each group.

The distributions of the responses of QoL questions for patients with HFrEF, HFnEF or No HF are shown in Tables 2.1 and 2.2. This showed a broadly similar pattern in patients with different heart failure phenotypes. There was also an extensive overlap in symptomatology between

Table 1
Baseline characteristics by patient groups: patients with HFrEF (LVEF < 40% or LVI > mild), patients with HFnEF (LVEF ≥ 40% or LVI ≤ mild but NT-proBNP > 400 ng/L) and patients with no HF (LVI ≤ mild and NT-proBNP ≤ 400 ng/L).

	Missing values	HF (n = 626)			HF (n = 626)	No HF (n = 405)	p-Value
		HFrEF (n = 377)	HFnEF (n = 249)	p-Value			
Age (years)	0	69 (11)	74 (9)	<0.001	71 (10)	67 (10)	<0.001
Men (%)	0	77%	54%	<0.001	65%	233 (58%)	0.001
IHD (%)	0	64%	39%	<0.001	54%	159 (39%)	<0.001
Diabetes (%)	131	19%	21%	0.461	20%	50 (14%)	0.037
BMI (kg/m^2)	0	27.1 (24.4–30.3)	27.4 (24.3–31.3)	0.336	27.2 (24.3–30.8)	29.0 (26.1–32.7)	<0.001
COPD (%)	0	7%	10%	0.170	8%	6%	0.395
AF (%)	0	17%	43%	<0.001	27.3%	1%	<0.001
QRS width (ms)	41	112 (98–142)	96 (86–110)	<0.001	104 (92–126)	92 (82–101)	<0.001
LVI > mild (%)	0	100%	0	<0.001	60%	0	<0.001
Left atrial dimension (cm)	0	4.4 (4.0–4.9)	4.2 (3.9–4.9)	0.637	4.3 (3.9–4.9)	3.8 (3.4–4.1)	<0.001
MR > mild (%)	106	125 (35%)	58 (25%)	0.013	31%	2%	<0.001
NT-proBNP (ng/L)	0	1592 (652–3718)	1194 (728–2338)	0.079	1389 (678–3049)	127 (68–212)	<0.001
NT-proBNP (ng/L) in sinus rhythm	0	1135 (493–2925)	1044 (639–1880)	0.931	1104 (566–2558)	120 (68–211)	<0.001
Sodium (mmol/L)	0	140 (137–141)	140 (137–141)	0.663	140 (137–141)	140 (138–141)	<0.001
Potassium (mmol/L)	7	4.4 (4.1–4.7)	4.4 (4.0–4.8)	0.466	4.4 (4.1–4.7)	4.3 (4.0–4.6)	0.001
Urea (mmol/L)	0	6.7 (5.3–9.6)	6.8 (5.2–9.4)	0.607	6.8 (5.3–9.5)	5.3 (4.3–6.5)	<0.001
Creatinine (μmol/L)	0	107 (89–135)	103 (87–129)	0.126	106 (87–132)	88 (77–101)	<0.001
eGFR (mL/min/1.73 m^2)	8	61 (45–73)	57 (45–72)	0.166	59 (45–72)	72 (61–83)	<0.001
Hb (g/dL)	0	13.7 (12.4–14.7)	13.2 (11.8–14.3)	0.002	13.5 (12.3–14.5)	14.1 (13.2–15.0)	<0.001
Loop diuretics (%)	19	74%	67%	0.045	71%	32%	<0.001
ACEi (%)	19	73%	54%	<0.001	66%	40%	<0.001
ARB (%)	19	7%	7%	0.999	7%	6%	0.630
BB (%)	19	56%	48%	0.035	53%	39%	<0.001
Digoxin (%)	19	16%	29%	<0.001	21%	2%	<0.001
Spironolactone (%)	19	23%	10%	<0.001	18%	2%	<0.001

LVI: left ventricular impairment; IHD: ischemic heart disease; BMI: body mass index; Hb: haemoglobin; BB: beta blocker.