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Neil Oldridge
University of Wisconsin - Milwaukee

Stefan Höfer
Innsbruck Medical University

Hannah McGee
Royal College of Surgeons in Ireland

Ronán Conroy
Royal College of Surgeons in Ireland

Frank Doyle
Royal College of Surgeons in Ireland, fdoyle4@rcsi.ie

See next page for additional authors

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Authors
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The HeartQoL: I. Development of a new core health-related quality of life questionnaire for patients with ischemic heart disease

Neil Oldridge [a]
Stefan Höfer [b]
Hannah McGee [c]
Ronan Conroy [d]
Frank Doyle [c]
Hugo Saner [e]
for the HeartQoL Project investigators

a. University of Wisconsin School of Medicine & Public Health and Aurora Cardiovascular Services, Aurora Sinai/Aurora St. Luke's Medical Center, Milwaukee, Wisconsin, USA
b. Department of Medical Psychology, Innsbruck Medical University, Innsbruck, Austria
c. Division of Population Health Sciences (Psychology), Royal College of Surgeons in Ireland, Dublin, Ireland
d. Division of Population Health Sciences (Epidemiology & Public Health Medicine), Royal College of Surgeons in Ireland, Dublin, Ireland
e. Cardiovascular Prevention and Rehabilitation, Swiss Cardiovascular Center Bern, Bern University Hospital, University of Bern, Bern, Switzerland

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Address for correspondence:

Neil Oldridge, PhD

Clinical Professor of Medicine
University of Wisconsin School of Medicine & Public Health and
Aurora Cardiovascular Services
960 North 12th Street, Suite 400
Milwaukee, WI 53217

Email: neilb@uwm.edu

ABSTRACT

Background

Evaluation of health-related quality of life (HRQL) is important in improving the quality of patient care.

Methods

The HeartQoL Project, with cross-sectional and longitudinal phases, was designed to develop a core ischemic heart disease (IHD) specific HRQL questionnaire, to be called the HeartQoL, for patients with angina, myocardial infarction (MI), or ischemic heart failure. Patients completed a battery of questionnaires and Mokken scaling analysis was used to identify items in the HeartQoL questionnaire.

Results

We enrolled 6,384 patients (angina, n=2,111, 33.1%; MI, n=2,351, 36.8%; HF, n=1,922, 30.1%) across 22 countries and 15 languages. The HeartQoL questionnaire comprises 14-items with 10-item physical and 4-item emotional subscales which are scored from 0 (poor HRQL) to 3 (better HRQL) with a global score if needed. The mean baseline HeartQoL global score was 2.2 (±0.5) in the total group and was different ($p<0.001$) by diagnosis (MI, 2.4 ±0.5; angina, 2.2 ±0.6; and heart failure, 2.1 ±0.6).

Conclusion

The HeartQoL questionnaire, with global and subscale scores, has the potential to allow clinicians and researchers to a) assess baseline HRQL, b) make between-diagnosis comparisons of HRQL, and c) evaluate change in HRQL in patients with angina, MI, or heart failure with a single IHD-specific HRQL instrument.

Keywords: Ischemic heart disease; angina; myocardial infarction; heart failure; health-related quality of life

INTRODUCTION

As one means to improve the quality of health care, the Institute of Medicine has emphasized the need for more patient-centered care [1]. Both the European Medicines Agency [2] and the US Food and Drug Administration [3] have defined evaluations or reports of a patient's health condition that come directly from the patient, such as health-related quality of life (HRQL), as patient-reported outcomes. Patient-reported outcomes are valuable in national and international clinical and research studies for assessing achievement of health goals, assessing health disparities between population segments, evaluating health care intervention effectiveness, and making between-diagnosis treatment comparisons. Specific HRQL questionnaires are designed for patients with either a specific disease or a specific diagnosis within a given disease [4]. However, this precludes between-diagnosis HRQL outcome comparisons. Core disease-specific HRQL questionnaires provide a solution to this limitation; for example, between-diagnosis HRQL comparisons have been possible for two decades in patients with different cancer diagnoses [5, 6].

Ischaemic heart disease (IHD) accounts for approximately 15.4% of all deaths in Europe [7] and 15.8% in the USA [8]. Patients with IHD, specifically angina, myocardial infarction (MI), and ischemic heart failure, present on a continuum of disease. With a wide range of health status deficits, IHD treatment and therapeutic goals include reduced mortality and an enhanced quality of the longer life. The National Heart, Lung and Blood Institute has stressed the importance of patient-reported outcomes in clinical care and relevant clinical trials for patients with IHD [9]. While valid and reliable IHD diagnosis-specific health status and HRQL tools are available for patients with angina, MI, and heart failure, no valid core IHD-specific HRQL instrument was available at the time the present project was initiated.

The HeartQoL Project was designed to develop and validate a core IHD-specific HRQL instrument for making between-diagnosis comparisons following interventions such as revascularization or cardiac rehabilitation that are routinely used in more than one IHD diagnosis.

The purpose of this paper is to describe the development of a core IHD-specific HRQL questionnaire, called the HeartQoL questionnaire, with psychometric properties described in a following paper.

METHODS

The HeartQoL Project was conducted between 2002 and 2011 in five regions (Eastern, Northern, Southern, and Western European regions and an English-speaking region) with a total of 22 countries where 15 languages are spoken: Danish, Dutch, English (Australia, Canada, Ireland, United Kingdom, and the United States of America), French, Flemish, German (Austria, Germany, and Switzerland), Hungarian, Italian, Norwegian, Polish, Portuguese, Russian, Spanish (Cuba and Spain), Swedish, and Ukrainian [10]. Each of the sites (n=54) received local Ethics Committee or Institutional Review Board approval.

The study was conducted in two phases: 1) a cross-sectional survey phase with three validated IHD-specific HRQL questionnaires to identify items for inclusion in the HeartQoL questionnaire and described in this manuscript; 2) a second phase to test the questionnaire's psychometric properties (described in a separate manuscript [11]).

Patients

The target in the cross-sectional study was to enroll at least 315 patients (105 with angina, 105 with MI and 105 with heart failure) speaking each of 15 languages, i.e., a sample size of at least 4,725 patients [10]. Physicians referred patients if they met the following eligibility criteria:

a. Experienced a documented MI between 1-6 months previously; or

b. Currently treated for angina (Canadian Cardiovascular Society class II, III or IV) with an objective measure of IHD (previous MI, exercise testing, echocardiogram, nuclear imaging or angiography); or

c. Currently treated for ischaemic heart failure (New York Heart Association Class II, III, or IV) with evidence of left ventricular dysfunction (ejection fraction <40% by invasive or non-invasive testing) and an objective measure of IHD (previous MI, exercise testing, echocardiogram, nuclear imaging or angiography), and

d. Were ≥18 years old and considered by the referring physician to 1) be able to complete the self-administered battery of HRQL instruments in the particular language, 2) not have serious

psychiatric disorder, and 3) not be a current substance abuser.

Patient-reported outcome assessment

The referring clinician identified their patient's clinical characteristics. All patients completed a battery of patient-reported questionnaires. This included a sociodemographic questionnaire, the Short-Form 36 (SF-36) [12, 13], the Hospital Anxiety and Depression Scale (HADS) [14, 15], and three validated IHD-specific questionnaires selected as the foundation of to-be-developed HeartQoL questionnaire, the Seattle Angina Questionnaire (SAQ) [16, 17], the MacNew Heart Disease Health-related Quality of Life Questionnaire (MacNew) [18, 19], and the Minnesota Living With Heart Failure (MLHF) Questionnaire [20, 21]. The SAQ and MLHF diagnosis-specific cues ("due to chest pain, chest tightness, or angina …" and "how your heart failure …", respectively) were both modified, with author permission, to "how your heart problem …". The MacNew timeframe was modified, also with permission, from "2 weeks" to "4 weeks" to complement the timeframe used in the SAQ and MLHF. Each questionnaire was either a) available in one of the 15 different languages or b) when language-specific translations were not available, accepted linguistic translation techniques such as forward-backward translation were used to translate the questionnaires [22]. Two independent translators, one a health care professional and the other a non-health care person and fluent in each language and English, were used to develop necessary questionnaires.

<u>Instrument development and item reduction</u>

Only the SAQ, MacNew, and MLHF items designated as physical, emotional, or social domain items were considered for the candidate pool of items as they are central to the assessment of HRQL [4]. The item reduction process consisted of two stages, first ranking the candidate pool items using the clinical impact method [23] and then using Mokken scaling to derive scales [24, 25].

1. Clinical impact method

The clinical impact method [23] asks patients to identify symptoms, activity limitations, and feelings that bother them in their everyday lives with the clinical impact score the product of the proportion bothered by an item and the "bothersomeness" score for that item on a scale from 1 to 5 ('little' to 'very' bothered). If a patient had responded affirmatively to an item but had given no "bothersomeness" score, it was imputed conservatively as follows. Item scores ranging from "little to very bothered" on the original questionnaire were given a "bothersomeness" score = 1. If the "bothersomeness" score was missing and the patient's response on the original questionnaire was "not bothered", those items were given a score = 0. Items with scores ≥ 1.00 were included in the candidate pool of items for Mokken scaling.

2. Mokken scaling

Mokken scale analysis, a hierarchical scaling method similar to Guttman scaling, 1) examines items in the candidate item pool for an underlying latent attribute represented by a set of items, 2) orders these items by degree of difficulty, and 3) uses an iterative selection procedure to form scales [24, 25]. Loevinger's H-coefficients measure the relationship between the numbers of Guttman observed errors and errors expected by chance. By convention, strong Mokken scales are indicated by H-coefficients ≥0.5, 0.49 to 0.40 for moderate, and 0.39 to 0.30 for weak scales [24, 25]. Item and subscale thresholds of H ≥0.5 were set; both subscale and global scale H-values were determined.

3. Formatting the HeartQoL questionnaire

The HeartQoL items are introduced with the following preamble: "We would like to know how your heart problem has bothered you and how you have been feeling during the last 4 weeks". The HeartQoL response options were determined with item characteristic curve modeling [26] with scores ranging from 0 to 3, higher scores indicating better HRQL.

RESULTS

International cohort (Table 1)

A cohort of 6,384 patients, living in 5 different geographical regions (22 countries with 54 sites in total) and speaking one of 15 languages, was enrolled in the HeartQoL Project; Eastern Europe (n=1,307 patients), Northern Europe (n=1,022 patients), Southern Europe (n=1,132 patients), Northern Europe (n=1,449 patients), and an English-speaking region (n=1,474 patients). Patients were referred with a diagnosis of angina (n=2,110; 33%), MI (n=2,350; 37%), or heart failure (n=1,920; 30%) meeting the project target of enrolling approximately equal proportions in each diagnosis.

Self-report sociodemographic and risk factors (Table 2)

Women made up 25% (n=1,694) of the cohort and the mean age in the total group was 62.5 years (SD= 11.3). The oldest patients were those with heart failure. Patients with angina were significantly less likely to be men or to smoke but more likely to report hypertension or high cholesterol and have a higher BMI than either patients with MI or patients with HF. Patients with MI were significantly more likely to be younger, to report being diabetic, and less likely to be inactive than patients with either angina or HF.

Health status, anxiety and depression (Table 2)

a. SF-36:

The mean physical and mental component summary (PCS and MCS, respectively) scores were below the population norm of 50 with lower PCS than MCS scores in all cases. Patients with MI had significantly higher PCS scores than patients with angina who had higher scores than patients with heart failure. There were no significant between-diagnosis MCS score differences.

b. HADS:

Patients with MI had significantly lower anxiety and depression scores than patients with either angina or heart failure and were also least likely to have depression scores >7 (19%)

although most likely to report anxiety scores >7 (39%). Patients with heart failure had lower anxiety scores than patients with angina while the opposite was true for depression.

Clinical Impact Method (Table 3)

A candidate pool of 26 items (physical, n= 14; emotional, n= 8; social, n= 4; SAQ, n= 5; MacNew, n= 13; MLHF, n= 8) with clinical impact scores ≥ 1.0 was identified for the Mokken scaling analysis.

a. SAQ

Two of the 9 eligible SAQ items, items #9 (strenuous sports) and #7 (running or jogging), were considered inappropriate for most patients with IHD. Four items had clinical impact scores ≥ 1.0 and, to capture a full range of physical activities, we included item #2 ('walk indoors on level'; clinical impact score = 0.26) in the candidate pool for Mokken analysis.

b. MacNew

Sixteen of the 27 eligible MacNew items had clinical impact scores ≥ 1.0. Items #4 ('down in the dumps'), #6 ('worn out'), and #9 ('short of breath') had lower scores than similar MLHF items (#21, #13, and #12) and were excluded from the candidate pool for Mokken analysis.

c. MLHF

Nine of the 13 eligible MHLF items had a score ≥ 1.0. Item #3 ('walking or climbing stairs') was excluded from the item candidate pool for Mokken analysis with a lower score than the corresponding SAQ item (#4).

Scale building (Tables 3)

Mokken analysis, with a threshold H-value ≥0.50 ("strong" scale), was used to build the HeartQoL from the candidate pool of the 26 items. Mokken analysis identified a bi-dimensional instrument with a 10-item physical subscale (H= 0.56) and a 4-item emotional subscale (H =0.54) (Table 3). Without setting an H threshold, the overall HeartQoL questionnaire with all 14 items (H-value ≥0.50), i.e., the global score, had a uni-dimensional H-value = 0.47 (Table 3

HeartQoL scores (Table 4)

On a HeartQoL scale response of 0 to 3, higher scores indicate better HRQL. Mean baseline HeartQoL global score in the group as a whole was 2.2 ±0.5; mean global scores were highest in patients in patients with MI (2.4 ±0.5), significantly higher ($p<0.001$) than in patients with angina (2.2 ±0.6) that, in turn, were significantly higher ($p<0.001$) than in patients with heart failure (2.1 ±0.6). A similar pattern by diagnosis was seen in the physical HeartQoL subscale; emotional subscale scores were highest in patients with MI but were not different in patients with angina or heart failure.

DISCUSSION

The HeartQoL questionnaire is a new 14-item IHD-specific core HRQL questionnaire based on the items in the SAQ, the MacNew, and the MLHF, with data provided by a cohort of 6,384 patients living in one of 22 countries with approximately equal numbers of patients with angina, MI, or ischemic heart failure. The HeartQoL appears to have potential as a core IHD-specific HRQL questionnaire demonstrating that patients with MI have a significantly better HRQL than patients with angina who in turn have a significantly better HRQL than patients with heart failure. The evidence for the validity of the HeartQoL questionnaire will be presented in a separate manuscript.

The 14 items in the HeartQoL scale cluster as a bi-dimensional questionnaire with a 10-item HeartQoL physical and a 4-item HeartQoL emotional subscale providing a global assessment and evaluation of how much a patient with angina, MI, or heart failure perceives he or she is bothered by their heart disease. Conventionally, HRQL consists of at least three domains, a physical, an emotional, and a social domain [4]. However, although four MacNew social domain items met the clinical impact score inclusion criteria for the 26-item candidate item pool these were not included among the 14 items underlying the bi-dimensional latent HRQL HeartQoL construct as determined by Mokken analysis. It appears that that whatever social problems these patients with IHD may have, they are not sufficiently unique or strong enough to form an independent latent construct. Alternatively, the MacNew social items may be culture- or diagnosis-specific, and thus do not generalize across the three IHD diagnostic groups assessed in this study.

There has been global explosion of interest in HRQL instruments as outcomes both in clinical practice but also in national and international research endeavors. We therefore designed the HeartQoL Project as an international effort and communicated our interest in conducting the project to members of the European Association of Cardiovascular Prevention and Rehabilitation. Volunteer investigators from 22 different countries agreed to enroll patients who met the project eligibility criteria that, among other factors, required 15 different language versions of the battery of

patient-reported questionnaires. Although the lack of language translations may be considered a limitation of the project, accepted linguistic translation techniques such as forward-backward translations were used where language versions were unavailable [22]. Although another limitation of the project may be the length of time it took to enroll all 6,384 patients, all site investigators were volunteers using their own and their staff time and effort to recruit patients.

There has been a proliferation of HRQL instruments in the past two or three decades with widely varying methods of development, content, breadth of use, and quality principles and psychometric property criteria to carry out instrument assessments have been published [27]. Guidelines for key psychometric attributes of HRQL instruments such as the HeartQoL include the conceptual and measurement model, reliability, validity, responsiveness, and respondent and administrative burden [27] and these are the focus of a separate manuscript [11].

CONCLUSIONS

The HeartQoL questionnaire is a new 14-item, international core IHD-specific assessment and evaluation system of the impact of cardiac interventions on patient-reported HRQL that has the potential to have an impact on the quality of patient care in the future. The psychometric properties of the HeartQoL questionnaire, with a global score and two subscales, will need to be demonstrated before it can be used by clinicians and researchers to a) assess baseline HRQL, b) make between-diagnosis comparisons of HRQL, and c) evaluate change in HRQL in patients with angina, MI, and heart failure.

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The Authors declare that there is no conflict of interest

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Table 1. Numbers of patients by region, country within region and by diagnosis [angina, myocardial infarction, and heart failure]

Region [sites]	Country	Diagnosis			
		IHD (n)	Angina (n)	Myocardial infarction (n)	Heart failure (n)
Total cohort (54)		6,384	2,111	2,351	1,922
Eastern Europe (4)		1,307	442	443	422
	Hungary	330	106	117	107
	Poland	332	115	112	105
	Russia	322	110	107	105
	Ukraine	323	111	107	105
Northern Europe (6)		1,022	349	362	311
	Denmark	364	142	117	105
	Norway	335	105	125	105
	Sweden	323	102	120	101
Southern Europe (13)		1,132	366	451	315
	Italy	327	105	117	105
	Portugal	354	113	136	105
	Spain + Cuba	451	148	198	105
Western Europe (16)		1,449	433	590	426
	Austria, Germany, Switzerland	365	116	143	106
	Belgium	348	105	137	106
	France	374	106	159	109
	Netherlands	362	106	151	105
English-speaking (15)		1,474	521	505	448
	Australia	296	77	111	108
	Canada	352	105	142	105
	UK + Ireland	357	117	131	109
	USA	469	222	121	126

Table 2. Self-report sociodemographic, risk factors, and Short-form-36 –Version 1 (SF-36) and Hospital Anxiety and Depression Scale (HADS) mean scores (standard deviation) or proportion in the total group and in patients with angina (AP), myocardial infarction (MI), or heart failure (HF)

Demographic & risk factors	Total Group (n= 6,380)	AP (n= 2,110)	MI (n= 2,350)	HF (n= 1,920)	p-value *
Age (years)	62.5 (11.3)	63.1 (10.2)	59.7 (11.4)	65.1 (11.5)	<0.001[a,b,c]
Male	75.2%	72.4%	75.9%	77.2%	<0.001[a,c]
Hypertension [¶]	55.5%	63.9%	50.0%	52.7%	<0.001[a,c]
Diabetes [¶]	20.9%	22.7%	15.4%	25.7%	<0.001[a,b]
Hypercholesterol [¶]	59.5%	67.2%	57.7%	53.1%	<0.001[a,c]
Smoking	15.1%	13.3%	16.7%	15.1%	<0.01[a,c]
BMI	27.4 (5.0)	28.0 (5.0)	26.9 (4.7)	27.3 (5.3)	<0.001[a,c]
Physical inactivity [¶¶]	69.9%	69.8%	65.4%	75.8%	<0.001[b,c]
Questionnaires					
SF-36					
PCS	39.1 (10.3)	37.9 (9.8)	43.1 (9.7)	35.5 (10.0)	<0.001[a,b,c]
MCS	47.1 (11.0)	46.8 (11.0)	47.4 (10.9)	47.1 (11.2)	= 0.17
HADS					
Anxiety	6.3 (4.1)	6.8 (4.0)	5.8 (4.1)	6.3 (4.2)	<0.001[a,b,c]
% anxious [§]	34.6%	30.4%	38.6%	35.2%	<0.001[a,b,c]
Depression	5.1 (3.8)	5.3 (3.7)	4.4 (3.7)	5.8 (3.9)	<0.001[a,b,c]
% depressed [§]	25.1%	25.7%	19.2%	31.8%	<0.001[a,b,c]

* p-value between-diagnosis with ANOVA (post-hoc Bonferroni correction; with non-homogeneous variances, Welch's F-statistic and post-hoc Games Howell correction) and Chi-square for proportions
a, MI vs. AP; b, MI vs. HF; c, AP vs. HF
¶ As told by his/her physician;
¶¶ Active on <3 occasions per week
§ HADS score >7

Table 3. Candidate item pool (n=26) from the Seattle Angina, MacNew, Minnesota Living with Heart Failure questionnaires and the items (n=14) included in the HeartQoL questionnaire (physical and emotional subscales); % (proportion bothered); bother score (mean); CIS ≥1.00 [clinical impact score; % * bother); H-values bi (bi-dimensional subscales) and uni (uni-dimensional scale)

Candidate Pool Items	%	Bother score	CIS ≥1.00	H-value bi	H-value uni
Physical subscale				**0.56**	**--**
Lift, move heavy objects, e.g., furniture, children *	69.4	3.2	2.2	0.55	0.49
Sports/exercise limited ‡	69.9	2.9	2.0	0.52	0.47
Tired, fatigued, low on energy ¶	70.2	2.7	1.9	0.56	0.55
Walking > a block at a brisk pace *	57.7	2.9	1.7	0.60	0.52
Physically restricted ‡	62.3	2.6	1.6	0.53	0.49
Climb, flight stairs without stopping *	58.5	2.7	1.6	0.58	0.51
Short of breath ¶	54.0	2.9	1.6	0.53	0.48
Garden, carry groceries *	51.8	2.6	1.3	0.62	0.54
House or yard work difficult ¶	38.9	2.8	1.1	0.59	0.52
Walk indoors on level **	11.7	2.2	0.26	0.52	0.46
Emotional subscale				**0.54**	**--**
Worry ¶	49.9	2.7	1.3	0.57	0.42
Not relaxed ‡	55.5	2.3	1.3	0.52	0.36
Frustrated ‡	48.8	2.6	1.3	0.51	0.38
Feel depressed ¶	40.0	2.6	1.0	0.58	0.42
H-value for uni-dimensional scale				**--**	**0.47**
Items >1.0 but not included					
Worn out ‡	64.8	2.6	1.7		
Sex ‡	44.7	3.2	1.4		
Sit or lie down ¶	54.1	2.6	1.4		
Sleeping well at night difficult ¶	47.0	3.0	1.4		
Restricted or limited ‡	58.0	2.4	1.4		
Unsure about exercise ‡	55.7	2.5	1.4		
Aching legs‡	52.8	2.6	1.4		
Chest pain ‡	50.9	2.5	1.3		
Confident ‡	49.3	2.5	1.3		
Difficult to concentrate, remember ¶	41.6	2.7	1.1		
Happy with personal life ‡	44.2	2.4	1.1		
Dizzy/lightheaded ‡	45.5	2.3	1.0		

* Seattle Angina item; ** Seattle Angina item included as an activity most patients were not bothered by; ‡ MacNew item; ¶ Minnesota Living with Heart Failure item

Table 4. HeartQoL health-related quality of life questionnaire mean (± standard deviation) scores in the total group and in patients with angina, myocardial infarction (MI), or heart failure

HeartQoL	Total Group (n=6,384)	Angina (n=2,111)	MI (n=2,351)	Heart failure (n=1,922)	p-value *
Physical score	2.2 (0.7)	2.2 (0.6)	2.4 (0.6)	2.0 (0.7)	<0.001 [a,b,c]
Emotional score	2.4 (0.6)	2.3 (0.6)	2.4 (0.6)	2.3 (0.7)	=0.003 [a,b]
Global score	2.2 (0.5)	2.2 (0.6)	2.4 (0.5)	2.1 (0.6)	<0.001 [a,b,c]

p-value between diagnosis with ANOVA (post-hoc Bonferroni correction; in case of inhomogeneous variances, Welch's F-statistic and post-hoc Games Howell correction) and with Chi-square for proportions

a, AP vs. MI; b, MI vs. HF; c, AP vs. HF