ELSEVIER

International Journal of Cardiology 139 (2010) 60–67

International Journal of Cardiology

www.elsevier.com/locate/ijcard

Quality of life predicts outcome in a heart failure disease management program

Christina O'Loughlin, Niamh F. Murphy, Carmel Conlon, Aoife O'Donovan, Mark Ledwidge, Ken McDonald *

Department of Cardiology, St Vincent's University Hospital, Elm Park, Dublin 4, Ireland

Received 28 January 2008; received in revised form 26 June 2008; accepted 2 September 2008
Available online 12 October 2008

Abstract

Background: Chronic heart failure (HF) is associated with a poor Health Related Quality of Life (HRQoL). HRQoL has been shown to be a predictor of HF outcomes however, variability in the study designs make it difficult to apply these findings to a clinical setting. The aim of this study was to establish if HRQoL is a predictor of long-term mortality and morbidity in HF patients followed-up in a disease management program (DMP) and if a HRQoL instrument could be applied to aid in identifying high-risk patients within a clinical context.
Methods: This is a retrospective analysis of HF patients attending a DMP with 18±9 months follow-up. Clinical and biochemical parameters were recorded on discharge from index HF admission and HRQoL measures were recorded at 2 weeks post index admission.
Results: 225 patients were enrolled into the study (mean age = 69 ± 12 years, male = 61%, and 78% = systolic HF). In multivariable analysis, all dimensions of HRQoL (measured by the Minnesota Living with HF Questionnaire) were independent predictors of both mortality and readmissions particularly in patients <80 years. A significant interaction between HRQoL and age ($Total_{(HRQoL)} * age$: $p < 0.001$) indicated that the association of HRQoL with outcomes diminished as age increased.
Conclusions: These data demonstrate that HRQoL is a predictor of outcome in HF patients managed in a DMP. Younger patients (<65 years) with a Total HRQoL score of ≥50 are at high risk of an adverse outcome. In older patients ≥80 years HRQoL is not useful in predicting outcome.

Keywords: Minnesota living with heart failure questionnaire; Heart failure; Disease management program; Health Related Quality of Life; Predictor

1. Introduction

Heart failure (HF) has been shown to reduce Health Related Quality of Life (HRQoL) to a greater extent than most other chronic diseases [1–3]. In patients with HF, poor HRQoL is associated with higher frequencies of hospital readmission [4–6] and death [4,6,7]. Furthermore, there is evidence to suggest that HRQoL is poorer in younger HF patients when compared to older patients [8].

Patient's perception of their own health status is increasingly being acknowledged to be as important as clinical and biological factors in predicting HF outcomes. HRQoL is recognized as a significant predictor of HF outcomes in a research environment however there has been little progress in developing the utility of these instruments within a clinical setting [9]. Progress in this area is difficult because of inconsistencies in the design of these research studies that make it difficult to generalize these results for practical use in a clinical setting [6,10]. Studies use different HRQOL questionnaires including global (e.g. The Medical Outcomes Study Short Form-36 (SF 36) questionnaire) and disease-specific instruments (e.g. Minnesota living with heart failure questionnaire[6,11] or the Kansas City Cardiomyopathy Questionnaire[12–15] and use different approaches to the multivariable modeling, employing

* Corresponding author. Tel.: +353 1 2304629; fax: +353 1 2304639.
E-mail address: kenneth.mcdonald@ucd.ie (K. McDonald).

0167-5273/$ - see front matter
doi:10.1016/j.ijcard.2008.09.003

different covariates and different outcomes. Given this, it is difficult to compare results across these studies.

While there have been prior studies examining the impact of HRQOL on outcome in HF populations[6,11–15] there have been no prior studies in HF patients attending a disease management program (DMP). Patients attending a DMP for HF have been shown to have an improved outcome [16,17] and better quality of life [16,18] than patients in routine care and therefore the impact of HRQOL in this population may not be similar.

The aim of this study is to examine the impact of HRQoL on outcome in HF patients attending a DMP which includes both older and younger patients and patients with systolic and preserved systolic function HF. In addition, we explore whether the disease-specific HF questionnaire (Minnesota living with heart failure) can be used to identify patients at higher risk of an adverse outcome and thus provide insight into how this instrument may be of clinical utility.

Table 1
Baseline demographics of the total sample and comparisons between those ≥65 versus <65 years of age.

Variable	Total	≥65 years	<65 years	*p*
(%)/Mean±standard deviation				
N	225	161(72)	64(28)	
Age (years)	69±12	76±7	54±9	N/A
Gender: male	138(61)	87(54)	51(79)	<0.001
Heart rate (bpm)	75±14	73±12	79±17	0.02
SBP/DBP (mm Hg)	118/69± 21/12	121/69± 21/12	112/69± 19/12	0.001/ 0.93
Ejection fraction (%)	36±13	37±13	31±11	0.003
LVSD (EF<45%)	176(78)	119(73)	57(89)	0.02
NYHA class: I&II	196(87)	135(84)	61(95)	0.02
Ischemic heart disease	141(63)	111(71)	30 (48)	0.002
Diabetes	47(21)	35(22)	12(19)	0.62
Pulmonary disease	45(20)	38(24)	7(11)	0.03
Arthritis	51(23)	47(29)	4(6)	<0.001
Cancer	16(7)	14(9)	2(3)	0.25
Medications				
ACE inhibitor and/or ARB	198(88)	138(86)	60(94)	0.09
Beta blocker	110(49)	74(46)	36(56)	0.12
Diuretic	194(86)	145(90)	49(77)	0.008
Nitrate	98(44)	85(53)	13(20)	<0.001
Biochemical markers				
Urea (mmol/L)	9.0±4.3	9.9±4.6	6.7±2.2	<0.001
Creatinine (μmol/L)	119.3±48.6	125.4±53.8	103.9±26.8	0.01
Sodium (mmol/L)	137.5±3.6	137.1±3.7	138.4±3.1	0.01
HRQoL scores				
Total HRQoL	47±24	47±23	49±25	0.29
Physical HRQoL	24±12	24±11	23±13	0.88
Emotional HRQoL	10±7	10±7	10±7	0.87

Abbreviated terms: N/A = Not Applicable; DBP = Diastolic Blood Pressure; SBP =Systolic Blood Pressure; NYHA = New York Heart Association Functional Classification; LVSD = Left Ventricular Systolic Dysfunction; ARB = Angiotensin Receptor Blocker; HRQoL = Health Related Quality of Life.

2. Materials and methods

2.1. Design

This is a retrospective analysis of survivors of a New York Heart Association (NYHA) class IV HF admission to St Vincent's University Hospital (1999–2005) who were subsequently followed-up in a hospital-based disease management program as described previously [19]. Patients with a class IV emergency HF admission were approached for enrolment into the DMP following stabilization of their condition. NYHA functional class IV HF was defined by a history and examination compatible with HF, dyspnea at rest, pulmonary edema on chest X-ray, Doppler-echocardiographic evidence of systolic or diastolic dysfunction and the need for parental therapy for at least 24 h. Inpatient care was provided by the specialist HF service. Excluded were patients with advanced malignancy, dementia, patients who did not have HF as their primary admitting diagnosis and those not deemed to have class IV HF on admission. Patients unable to participate for personal or geographical reasons and nursing home residents were also excluded. The investigation conforms with the principles outlined in the Declaration of Helsinki.

Baseline information including clinical (weight, systolic/diastolic blood pressure and heart rate) and biochemical parameters (renal profile), medical history and co-morbidities including pulmonary disease (having either asthma or chronic obstructive pulmonary disease (COPD) or both) were recorded on discharge from index admission by the HF nurse (see Table 1). The Minnesota Living with Heart Failure (MLHF) questionnaire was administered to patients within 2 weeks of discharge from index admission. NYHA functional classification was also recorded during index admission and within 2 weeks of discharge from index admission by a clinician.

2.2. Outcome measures

All-cause emergency readmissions were defined as any non-elective medical or surgical hospital admission including HF readmissions.

All-cause death was also examined.

2.3. Data collection

All data including index admission, all subsequent contacts and all events post index admission were recorded on a database. To ensure optimal collection of outcome measure data, patients and their families were advised to inform the unit of any hospital admission. The HF nurse requested information about the admission and determined the reason for its occurrence (hospital discharge letter/request for hospital notes). In addition, chart reviews and reviews of the database at St. Vincent's University Hospital were conducted to determine the cause of death and readmission. Patients were also interviewed about events at the clinic during their annual review. Patients lost to follow-up were contacted by phone or their general practitioners were contacted for information.

2.4. Health Related Quality of Life measurement

Health Related Quality of Life (HRQoL) was assessed using the Minnesota Living with Heart Failure (MLHF) questionnaire [20]. The MLHF is a disease-specific validated, self-administered questionnaire consisting of 21 questions that refer to limitations that patients frequently attribute to HF, and address the physical, social, emotional, dietary and economic limitations and the side effects of treatment. Patients rate the degree to which their HF has prevented them from living as they wanted to during the last month using a Likert-type scale ranging from 0 (no effect) to 5 (very much). Scores range from 0 (no effect) to 105 (worst possible score) in the Total HRQoL measure. The MLHF is a multidimensional instrument containing both a Physical (8-items: scores range from 0 to 40) and an Emotional (5-items: scores range from 0 to 25) dimension.

2.5. Statistical analysis

Demographics are presented as mean ± standard deviation (SD) for continuous variables and as frequencies and percents for categorical variables. Comparisons between those ≥ 65 years and < 65 years were made using *t*-test for continuous variables and chi square test for categorical variables (Table 1). When completing the questionnaire patients were asked to mark zero for any items that did not apply to them rather than leave missing data. A Multiple imputation procedure was employed using NORM statistical software to impute missing data (< 5%) [21].

Internal consistency/scale reliability of the MLHF was calculated using Cronbach's Alpha (α) where higher values (close to 1) indicate better scale reliability. NYHA classification I and II and classifications III and IV were grouped into two categories due to small samples. Systolic function was categorized into preserved systolic function (ejection fraction (EF) ≥ 45%) and left ventricular systolic dysfunction (LVSD) (EF < 45%). Differences in HRQoL across NYHA classes were analyzed using ANCOVA (adjusting for gender and age). Time-to-event-data were analyzed using the proportional hazards model [22]. A separate model was estimated for Total, Physical and Emotional HRQoL. Age, gender, NYHA functional classification, and LVSD were considered important clinically meaningful variables and included in the multivariable models irrespective of significance. Using hierarchical modeling, co-morbidities (pulmonary disease, arthritis, cancer, and diabetes mellitus), heart failure etiology (ischemic heart disease) and medications (ACE inhibitors and/or angiotensin receptor blockers (ARB), β-blockers, any diuretic, and nitrates) were introduced into the multivariable model in separate blocks. On selection of the final multivariable model, all excluded variables were re-introduced into the model individually to ensure significant confounders were not omitted. The *p* value of the partial likelihood ratio test was used to confirm if a covariate (or blocks of covariates) were significant and the coefficients of the remaining variables were assessed to determine if important (> 20%) changes had occurred on variable exclusion. The *p* value of this statistic was used in preference to the Wald statistic if conflict occurred as it is not biased to Type II errors when standard errors are large [22]. All clinically meaningful interactions were tested. Only significant variables are presented in the final models in Tables 2 and 4.

In order to evaluate clinically important HRQoL thresholds and the nature of the interaction effect between age and Total HRQoL, age was centered at five year intervals (55–80 years) and Total HRQoL was dichotomized using 10 point increments (Total HRQoL from 50–80). 50 was chosen as a starting point as the interaction effect was insignificant at Total HRQoL = 40. Hazard ratios and 95% confidence intervals were calculated and the multivariable model in Table 2 re-estimated incorporating the interaction term between the centered age variables and the dichotomized Total HRQoL variables respectively (Table 3). This also allowed us to compare risk of all-cause death between

Table 2
Independent predictors of all-cause deaths using the proportional hazards statistical model: comparison of the impact of the HRQoL dimensions as measured by the Minnesota Living with Heart Failure questionnaire. [a]

	Total	Physical	Emotional
HRQoL [b]	1.185(1.069, 1.313) ***	1.400(1.109, 1.767)**	1.618(1.170, 2.236)**
HRQoL^{X}Age (interaction)	0.998(0.997, 0.999)**	0.996(0.993, 0.999)**	0.994(0.990, 0.998)**
Age (years)	1.226(1.114, 1.350)***	1.218(1.100, 1.348)***	1.167(1.056, 1.254)***
Gender: male	2.068(1.092, 3.915)*	1.980(1.057, 3.709)*	2.118(1.124, 3.989)*
Creatinine (μmol/L)	1.006(1.001, 1.010)**	1.005(1.001, 1.010)*	1.006(1.002, 1.010)**
SBP (mm Hg)	0.982(0.967, 0.998)*	0.984(0.969, 1.000)*	0.983(0.990, 0.998)**
Model fit: χ^2 (*df*), *p*	34.0 (8), $p<0.001$	32.6 (8), $p<0.001$	31.8 (8), $p<0.001$

* $p \le 0.05$, ** $p \le 0.01$.*** $p<0.001$.
Abbreviated terms: HRQoL = Health Related Quality of Life; SBP = Systolic Blood Pressure.
[a] Additional variables included in the models were NYHA functional classification and Left ventricular systolic function. Neither of these were significant independent predictors of outcome.
[b] HRQoL is assessed in all multivariable models as a continuous variable.

Table 3
Hazard ratio and 95% confidence intervals of the interaction effect between age centered at key values and total Health Related Quality of Life dichotomized at 50, 60, 70 and 80: predicting all-cause deaths.

	Total Health Related Quality of Life			
	Hazard ratio (95% confidence intervals), *p* value			
Age (centered)	HRQoL ≥50	HRQoL ≥60	HRQoL ≥70	HRQoL ≥80
55 years	8.16(1.58,42.13), 0.01	8.80(2.17,35.70), 0.002	8.25(2.37, 28.74), 0.001	8.54(2.12, 34.43), 0.003
60 years	5.22(1.41, 19.26), 0.01	6.23(2.03,19.16), 0.001	6.08(2.24, 16.52), <0.001	6.53(2.16, 19.69), 0.001
65 years	3.34(1.24, 9.00), 0.02	4.42(1.86,10.57), 0.001	4.48(2.04, 9.84), <0.001	4.98(2.08, 11.93), <0.001
70 years	2.13(1.03, 4.43), 0.04	3.14(1.59,6.17) 0.001	3.30(1.73, 6.29), <0.001	3.81(1.79, 8.10), 0.001
75 years	1.36(0.76, 2.46), 0.30	2.22(1.22,4.04), 0.009	2.43(1.30, 4.54), 0.005	2.91(1.30, 6.49), 0.009
80 years	0.87(0.45, 1.68), 0.68	1.58(0.80,3.10), 0.19	1.79(0.86, 3.75), 0.12	2.22(0.83, 5.98), 0.11

patients at different ages and at different levels of Total HRQoL. This analysis was conducted for the outcome of all-cause death [22].

Patients who did not have an event and who had extended follow-up >2 years were censored at 2-years. SPSS (Statistical Package for the Social Sciences) statistical software version 12 was used to estimate these models.

3. Results

3.1. Patient population

Two hundred and twenty five patients completed the MLHF questionnaire at baseline (Table 1). The average age of the sample was 69±12 years with 28% <65 years of age. Sixty-one percent were male, 63% had an ischemic etiology, 83% were NYHA functional classification II, and 78% had left ventricular systolic dysfunction (EF<45%). The younger HF patients (<65 years) were significantly different from the older patients (≥65 years) with more males, higher heart rate, lower systolic blood pressure (SBP), less patients with ischemic etiology, lower EF, better NYHA functional classification, and lower urea and creatinine levels.

The internal consistency of the Physical ($\alpha=0.92$) and Emotional ($\alpha=0.85$) dimensions of the MLHF questionnaire indicated high scale reliability. There was no significant difference in average Total, Emotional and Physical HRQoL scores between the age groups (Table 1).

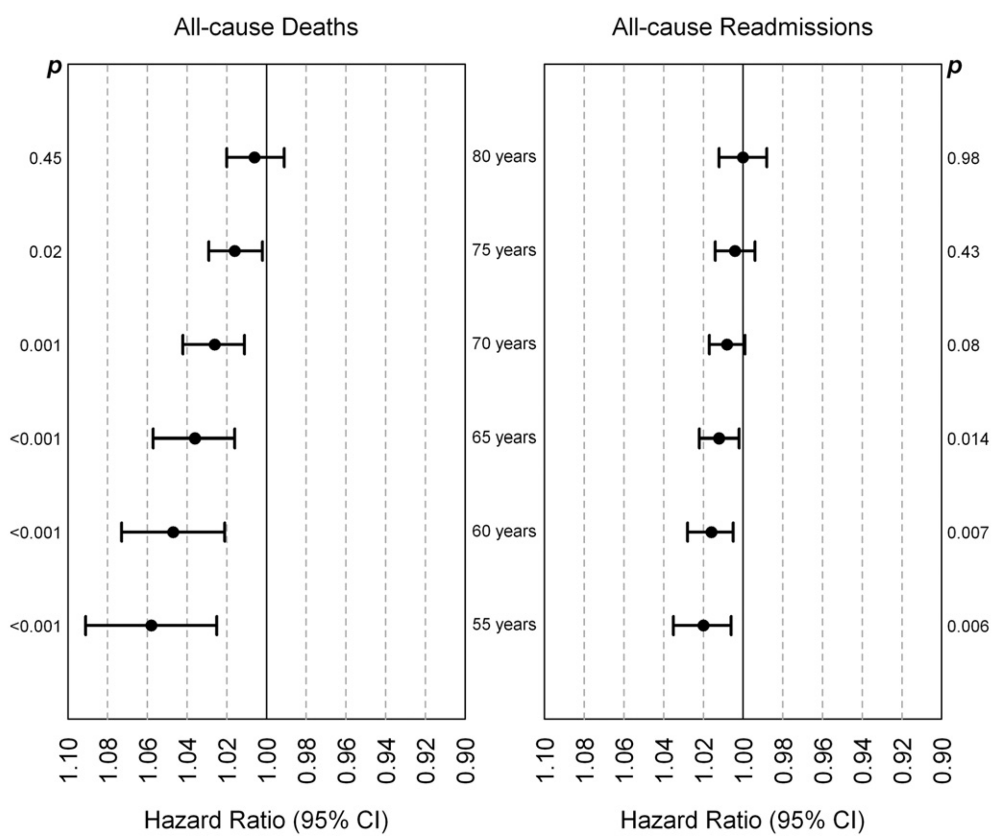

Fig. 1. The effect of Total HRQoL [(Hazard Ratios (HR) and 95% confidence intervals (CI)] on all-cause death and all-cause readmissions in different age groups (centered at 55, 60, 65, 70, 75 and 80 years).

3.2. All-cause deaths

Fifty-four (24%) patients died during the follow-up period (18±8 months). This comprised of 11% of patients aged <70 yrs, 35% of those aged between 70–79 years and 34% of those aged ≥80 years.

3.2.1. Univariable analysis

Univariable analysis identified the Total HRQoL (Hazard Ratio $_{(Total)}$ (HR): 1.012, 95% CI: 1.000, 1.024, $p<0.05$) and the Physical dimension of HRQoL ($HR_{(Physical)}$: 1.025, 95% CI: 1.000, 1.051, $p=0.05$) as significant unadjusted predictors of all-cause deaths. The Emotional dimension was not univariably significant ($HR_{(Emotional)}$: 1.032, 95% CI: 0.993, 1.072, $p=0.11$). Other unadjusted significant predictors of outcome were age (HR: 1.057, 95% CI: 1.027, 1.086, $p<0.001$), urea (HR:1.096, 95% CI: 1.050,1.143, $p<0.001$), creatinine (HR: 1.006 95% CI: 1.003, 1.010, $p<0.001$) and sodium (HR: 0.913, 95% CI: 0.854, 0.976, $p=0.008$).

3.2.2. Multivariable analysis

Each dimension of the MLHF questionnaire (Total, Physical and Emotional) was modeled individually and the results presented in Table 2.

Total HRQoL had a significant main effect on all-cause mortality (Table 2). A significant interaction effect between *Total HRQoL and age* in relation to this end point was observed meaning that the estimate of the effect of HRQoL on outcome is dependent on the age of the patient. Other independent predictors of survival were male gender, increased levels of creatinine and lower levels of systolic blood pressure (Table 2). All models were adjusted for the effects of NYHA functional classification and LVSD. Neither were significant. Using a hierarchical approach, we added the medications, co-morbidities, and HF etiology respectively in blocks to the multivariable model and found that none were significant within the blocks or individually when we tested for variable confounding. The same model was fit to both the Physical and Emotional dimensions with similar results (Table 2).

We examined the nature of the interaction effect by calculating point and interval estimates of the Hazard ratios (HRs) and 95% confidence intervals centered at key ages (Fig. 1: estimated for Total HRQoL only). The impact of Total HRQoL on outcome decreases as age increases, until the interaction effect becomes insignificant for patients aged 80 years and older.

The Total HRQoL variable was dichotomized at values in intervals of 10 starting at a Total HRQoL score of 50 using the same multivariable model as outlined in Table 2. This level was chosen as a starting point because the interaction effect between age and HRQoL was insignificant at a score of 40. For all levels of HRQoL the risk of death decreases as patients get older (Table 3). In general the risk of death is greater as HRQoL increases across all age groups. For younger patients this risk is very high at any of the cut off points on HRQoL (from 50–80), particularly for those ≤60 years of age. However confidence intervals are quite large which is probably reflective of smaller samples in the younger age groups so caution needs to be taken when interpreting the results. In addition, there is little differentiation between the hazard ratios across the cut off points however the risk of death is increasing as HRQoL levels increase. These results suggest that for patients' ≤60 years of age a Total HRQoL value of 50 or greater is a cause for concern. For those aged 65–70 years the risk is increased at levels of 50 but not to the same extent, and for those aged >75 years a score of 50 has little independent prognostic impact. As scores increase above 50 for older patients (>65 years), higher HRQoL scores are reflective of a greater risk of death. However, at 80 years of age HRQoL is not predicting risk even at levels of Total HRQoL≥80.

3.3. All-cause emergency readmissions

Within the 2 year follow-up period 116 (52%) of patients had at least one emergency all-cause readmission. Forty two percent ($n=42$) of patients aged <70 years, 62% ($n=52$) of those aged between 70–79 years and 54% ($n=22$) of those aged ≥80 years had an emergency readmission.

3.3.1. Univariable analysis

In univariable analysis, the Total ($HR_{(Total)}$: 1.010, 95% CI: 1.002, 1.019), the Physical ($HR_{(Physical)}$: 1.021, 95% CI: 1.004,

Table 4
Independent predictors of all-cause emergency readmissions using the proportional hazards statistical model: comparison of the impact of the HRQoL dimensions as measured by the Minnesota Living with Heart Failure questionnaire.[a]

	Total	Physical	Emotional
HRQoL[b]	1.068(1.011, 1.128)*	1.130(1.012, 1.262)*	1.349(1.115, 1.632)**
HRQoL^{X}Age (interaction)	0.999(0.998, 1.000)*	0.998(0.997, 1.000)*	0.996(0.993, 0.999)**
Age (years)	1.075(1.025, 1.128)**	1.070(1.021, 1.122)**	1.075(1.034, 1.117)**
Gender: male	1.570(1.029, 2.394)*	1.542(1.013, 2.348)*	1.620(1.060, 2.476)*
NYHA class: III & IV	1.817(1.109, 2.977)*	1.787(1.093, 2.921)*	1.979(1.202, 3.259)**
Cancer	2.104(1.162, 3.811)*	2.040(1.121, 3.712)*	2.033(1.123, 3.681)*
Model fit: χ^2 (df), p	29.8 (7), $p<0.001$	29.1 (7), $p<0.001$	32.2 (7), $p<0.001$

* $p\leq0.05$ **, $p\leq0.01$***, $p<0.001$.

[a] Left ventricular systolic dysfunction was also included in the model and was not a significant independent predictor of outcome.

[b] HRQoL is assessed in all multivariable models as a continuous variable.

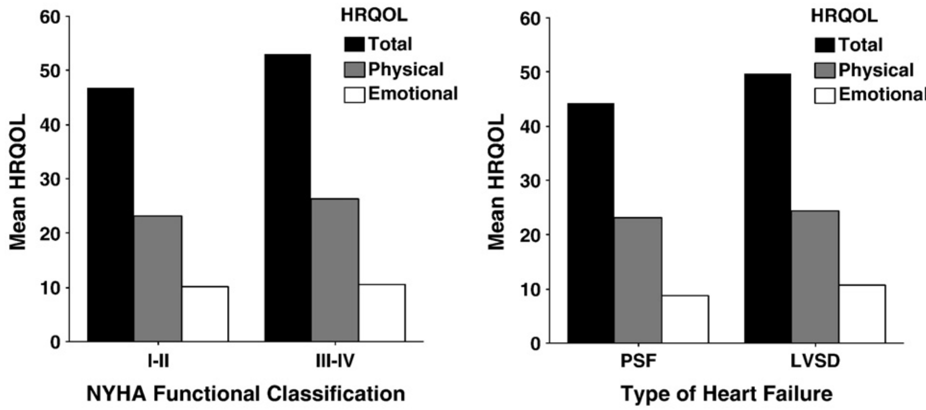

Fig. 2. Association of NYHA functional classification (class I&II versus III&IV) and type of HF (left ventricular systolic dysfunction: EF < 45% versus preserved systolic function: EF ≥ 45%) with HRQoL as measured by the Total, Physical and Emotional dimensions of the Minnesota Living with Heart Failure questionnaire (all $p > 0.05$: adjusting for age and gender).

1.038) and the Emotional ($HR_{(Emotional)}$: 1.032, 95% CI: 1.005, 1.059) HRQoL dimensions were all significant predictors of all-cause emergency readmissions. Other significant predictors of outcome were age (HR:1.020, 95% CI: 1.003, 1.037, $p = 0.02$), NYHA classification III&IV vs. I&II (HR: 1.988, 95% CI: 1.238, 3.192, $p = 0.004$), Pulmonary disease (HR: 1.576, 95% CI: 1.039, 2.389, $p = 0.03$), urea (HR: 1.054, 95% CI: 1.017, 1.093, $p = 0.004$) and creatinine (HR: 1.004, 95% CI: 1.001, 1.007, $p = 0.008$).

3.3.2. Multivariable analysis

The results of the multivariable analysis for the Total, Physical and Emotional dimensions of HRQoL are presented in Table 4. The Total HRQoL domain had a significant main effect on all-cause emergency readmission and there was a significant interaction effect between *Total HRQoL and age* on all-cause emergency readmission. The point and interval estimates (Fig. 1) show that the association of HRQoL with outcome diminishes as patients get older until the interaction effect becomes insignificant for patients aged 70 years and older. In addition, patients with a diagnosis of cancer and patients with NYHA functional classification III and IV were more likely to have an emergency readmission. LVSD, co-morbidities, ischemic heart disease, levels of urea or creatinine and medications were not predictive of readmission. Similar results were noted for the Physical and Emotional specifications of this model.

3.4. HRQoL and disease severity

Adjusting for age and gender effects, no significant differences were observed across NYHA functional class in either the Total, the Physical or the Emotional HRQoL scores (Fig. 2. all $p > 0.05$). Similarly, HRQoL scores (for all domains) did not distinguish between patients with left ventricular systolic dysfunction and patients with preserved systolic function (Fig. 2. all $p > 0.05$).

4. Discussion

This report has shown that HRQoL is a predictor of HF outcomes in patients followed-up in a DMP. Our results show that Total HRQoL and both the Physical and Emotional domains of HRQoL are significant independent predictors of long-term mortality and morbidity. However, the magnitude of this association with outcome diminishes as patients increase in age, becoming insignificant in older patients. Patients ≤ 60 years are at a high risk of an event when Total HRQoL scores are ≥ 50. The data indicate that in a 70 year old HF patient a HRQoL of 50 or more predicts a two fold increase in the risk of death. As total HRQoL increases the risk of an event similarly increases however in patients' ≥ 80 years HRQoL does not appear to be useful in predicting outcome. In contrast, NYHA classification was not a significant predictor of mortality nor did it differentiate between levels of HRQoL although it was an independent predictor of all-cause emergency readmissions. These results suggest that patients' perception of their condition on entering a DMP remains a more useful measure of disease severity and predictor of HF outcomes than NYHA classification. However, while further research is required HRQoL measures may have clinical utility for risk stratifying patients for more intensive follow-up.

Results from the majority of randomized control trials of DMPs generally agree that HRQoL levels significantly improve in patients assigned to DMP care of HF as compared to non-structured routine care [23]. It is believed that the relationship between HF status and HRQoL differs between older and younger patients. One study found that baseline HRQoL was significantly poorer in patients < 65 years versus patients ≥ 65 years of age [24]. However, it was thought that these results were explained by poorer NYHA status in the younger HF group. Our data showed no difference in the average HRQoL scores nor NYHA classification between those aged < 65 years versus ≥ 65 years.

The current literature indicates that poor HRQoL is related to higher frequencies of hospital readmission [4–6] and death [4,6,7] in non-structured, routine care of HF patients. To the best of our knowledge, this is the first report that demonstrates that HRQoL predicts outcome in patients' followed-up in a DMP. Patients attending a DMP for HF have been shown to have an improved outcome [16,17] and better quality of life [16,18] than patients in routine care. Furthermore, this report showed that the strength of the association of HRQoL with outcomes decreased as patients' increased in age. This significant interaction between age and HRQoL has not been reported previously. In older patients, the reason why HRQoL no longer is predictive of outcome remains unclear. This may be explained by older patients' accepting disease-related limitations as part of the natural ageing process. Of concern was the significantly increased risk of death in patients' ≤65 years with a Total HRQoL score ≥50. Our DMP includes a larger proportion of younger patients (28% <65 years) than similar studies [25]. It may be relevant that the disease profile of older and younger patients differed, with older patients more likely to have preserved systolic function and worse renal function. Furthermore, research has shown that depression, which is highly prevalent in HF patients, is more common in younger HF patients [26] and is associated with poor outcomes, declining health status and quality of life [27–29]. Depression also has a negative impact on compliance to HF treatment regimes which may help explain these findings [30].

Our results suggest that patient's self assessment of their functional status as measured by the MLHF is stronger than NYHA functional classification in predicting HF outcomes. These results are supported by the literature [31] with some studies showing the superiority of patients self assessment [32] in predicting outcomes when compared to clinicians assessment, although the literature is not unanimous [33–35]. In addition, the MLHF has been shown to have a poor association with NYHA class [36] which is in agreement with our findings. We also observed that HRQoL was not significantly different between patients with preserved systolic function and left ventricular systolic dysfunction, a finding which is supported by more recent studies [37]. The NYHA classification method of assessment has been criticized for being open to interpretation by the assessor, unstandardized and crude [38] which may explain this lack of association between clinician and patient measures of functional status.

4.1. Limitations

This study is limited by its retrospective design and consequently a number of variables that may be important in multivariable modeling were not assessed routinely at baseline in our study (including BNP, socioeconomic status and psychosocial measures such as anxiety, depression and medication adherence). Caution must also be taken in generalizing these results because of the relatively small sample size which may explain the large confidence intervals around the hazard ratios of patients' ≤65 years. Moreover, the fact that the vast majority of patients at baseline were in NYHA functional class II may explain why this variable was not a predictor of mortality or correlated with levels of HRQoL. In addition, our DMP excludes sicker patients who did not survive an admission or older patients that are in nursing homes or who suffer cognitive impairment, and thus may not be representative of HF patients in general although they would be representative of patients who attend a DMP. Finally, it would be of value to have sequential HRQoL assessments of patients to allow the examination of the direct impact of the DMP on the relationship between HRQoL and outcome.

5. Conclusion

This study has shown that HRQoL (Total, Physical and Emotional dimensions) is a strong indicator of mortality and emergency readmission in patients' attending a DMP. The unique observation of a significant interaction between HRQoL and age showed that this instrument is a stronger predictor of outcome in younger HF patients. A score of 50 in Total HRQoL in younger patients' is a cause for major concern. In a 70 year old HF patient a Total HRQoL score of ≥50 predicts a doubling of risk of death, while in very elderly patients HRQoL is not indicative of risk of outcome. Further studies, with a prospective design, a larger sample size and inclusive of younger HF patients are required. These should help to make the instrument clinically useful and aid clinicians in identifying those who could benefit from more intensive follow up.

Acknowledgement

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [39].

References

[1] Hobbs FD, Kenkre JE, Roalfe AK, Davis RC, Hare R, Davies MK. Impact of HF and left ventricular systolic dysfunction on quality of life: a cross-sectional study comparing common chronic cardiac and medical disorders and a representative adult population. Eur Heart J 2002 December;23(23):1867–76.

[2] Juenger J, Schellberg D, Kraemer S, et al. Health related quality of life in patients with congestive heart failure: comparison with other chronic diseases and relation to functional variables. Heart 2002 March;87 (3):235–41.

[3] Alonso J, Ferrer M, Gandek B, et al. Health-related quality of life associated with chronic conditions in eight countries: results from the International Quality of Life Assessment (IQOLA) Project. Qual Life Res 2004 March;13(2):283–98.

[4] Konstam V, Salem D, Pouleur H, et al. Baseline quality of life as a predictor of mortality and hospitalization in 5,025 patients with congestive heart failure. SOLVD Investigations. Studies of Left Ventricular Dysfunction Investigators. Am J Cardiol 1996 October 15;78(8):890–5.

[5] Stull DE, Clough LA, Van DD. Self-report quality of life as a predictor of hospitalization for patients with LV dysfunction: a life course approach. Res Nurs Health 2001 December;24(6):460–9.

[6] Rodriguez-Artalejo F, Guallar-Castillon P, Pascual CR, et al. Health-related quality of life as a predictor of hospital readmission and death among patients with heart failure. Arch Intern Med 2005 June 13;165 (11):1274–9.
[7] Hulsmann M, Berger R, Sturm B, et al. Prediction of outcome by neurohumoral activation, the six-minute walk test and the Minnesota Living with Heart Failure Questionnaire in an outpatient cohort with congestive heart failure. Eur Heart J 2002 June;23(11):886–91.
[8] Franzen K, Saveman BI, Blomqvist K. Predictors for health related quality of life in persons 65 years or older with chronic heart failure. Eur J Cardiovasc Nurs 2007 June;6(2):112–20.
[9] Rumsfeld JS. Health status and clinical practice: when will they meet? Circulation 2002 July 2;106(1):5–7.
[10] Johansson P, Dahlstrom U, Brostrom A. Factors and interventions influencing health-related quality of life in patients with heart failure: a review of the literature. Eur J Cardiovasc Nurs 2006 March;5(1):5–15.
[11] Alla F, Briancon S, Guillemin F, et al. Self-rating of quality of life provides additional prognostic information in heart failure. Insights into the EPICAL study. Eur J Heart Fail 2002 June;4(3):337–43.
[12] Heidenreich PA, Spertus JA, Jones PG, et al. Health status identifies heart failure outpatients at risk for hospitalization or death. J Am Coll Cardiol 2006 February 21;47(4):752–6.
[13] Soto GE, Jones P, Weintraub WS, Krumholz HM, Spertus JA. Prognostic value of health status in patients with heart failure after acute myocardial infarction. Circulation 2004 August 3;110 (5):546–51.
[14] Faller H, Stork S, Schowalter M, et al. Is health-related quality of life an independent predictor of survival in patients with chronic heart failure? J Psychosom Res 2007 November;63(5):533–8.
[15] Sullivan MD, Levy WC, Russo JE, Crane B, Spertus JA. Summary health status measures in advanced heart failure: relationship to clinical variables and outcome. J Card Fail 2007 September;13(7):560–8.
[16] McAlister FA, Lawson FM, Teo KK, Armstrong PW. A systematic review of randomized trials of disease management programs in heart failure. Am J Med 2001 April 1;110(5):378–84.
[17] Uretsky BF, Pina I, Quigg RJ, et al. Beyond drug therapy: nonpharmacologic care of the patient with advanced heart failure. Am Heart J 1998 June;135(6 Pt 2 Su):S264–84.
[18] Phillips CO, Singa RM, Rubin HR, Jaarsma T. Complexity of program and clinical outcomes of heart failure disease management incorporating specialist nurse-led heart failure clinics. A meta-regression analysis. Eur J Heart Fail 2005 March 16;7(3):333–41.
[19] McDonald K, Ledwidge M, Cahill J, et al. Elimination of early rehospitalization in a randomized, controlled trial of multidisciplinary care in a high-risk, elderly heart failure population: the potential contributions of specialist care, clinical stability and optimal angiotensin-converting enzyme inhibitor dose at discharge. Eur J Heart Fail 2001 March;3(2):209–15.
[20] Rector TS, Cohn JN. Assessment of patient outcome with the Minnesota Living with Heart Failure questionnaire: reliability and validity during a randomized, double-blind, placebo-controlled trial of pimobendan. Pimobendan Multicenter Research Group. Am Heart J 1992 October;124(4):1017–25.
[21] Schafer JL. NORM: Multiple imputation of incomplete multivariate data under a normal model, version 2; 1999. Software for Windows 95/98/NT, available from http://www.stat.psu.edu/~jls/misoftwa.html.
[22] Hosmer D, Lemeshow S. Applied Survival Analysis: Regression Modeling of Time to Event Data. New York: John Wiley & Sons, Inc; 1999.
[23] McAlister FA, Stewart S, Ferrua S, McMurray JJ. Multidisciplinary strategies for the management of heart failure patients at high risk for admission: a systematic review of randomized trials. J Am Coll Cardiol 2004 August 18;44(4):810–9.
[24] Hou N, Chui MA, Eckert GJ, Oldridge NB, Murray MD, Bennett SJ. Relationship of age and sex to health-related quality of life in patients with heart failure. Am J Crit Care 2004 March;13(2):153–61.
[25] Franzen K, Saveman BI, Blomqvist K. Predictors for health related quality of life in persons 65 years or older with chronic heart failure. Eur J Cardiovasc Nurs 2007 June;6(2):112–20.
[26] Freedland KE, Rich MW, Skala JA, Carney RM, vila-Roman VG, Jaffe AS. Prevalence of depression in hospitalized patients with congestive heart failure. Psychosom Med 2003 January;65(1):119–28.
[27] Jiang W, Alexander J, Christopher E, et al. Relationship of depression to increased risk of mortality and rehospitalization in patients with congestive heart failure. Arch Intern Med 2001 August 13;161 (15):1849–56.
[28] Vaccarino V, Kasl SV, Abramson J, Krumholz HM. Depressive symptoms and risk of functional decline and death in patients with heart failure. J Am Coll Cardiol 2001 July;38(1):199–205.
[29] Rumsfeld JS, Havranek E, Masoudi FA, et al. Depressive symptoms are the strongest predictors of short-term declines in health status in patients with heart failure. J Am Coll Cardiol 2003 November 19;42 (10):1811–7.
[30] Morgan AL, Masoudi FA, Havranek EP, et al. Difficulty taking medications, depression, and health status in heart failure patients. J Card Fail 2006 February;12(1):54–60.
[31] Mejhert M, Kahan T, Persson H, Edner M. Predicting readmissions and cardiovascular events in heart failure patients. Int J Cardiol 2006 April 28;109(1):108–13.
[32] Ekman I, Cleland JG, Swedberg K, Charlesworth A, Metra M, Poole-Wilson PA. Symptoms in patients with heart failure are prognostic predictors: insights from COMET. J Card Fail 2005 May;11 (4):288–92.
[33] Komajda M, Lapuerta P, Hermans N, et al. Adherence to guidelines is a predictor of outcome in chronic heart failure: the MAHLER survey. Eur Heart J 2005 August;26(16):1653–9.
[34] Pocock SJ, Wang D, Pfeffer MA, et al. Predictors of mortality and morbidity in patients with chronic heart failure. Eur Heart J 2006 January;27(1):65–75.
[35] Subramanian U, Weiner M, Gradus-Pizlo I, Wu J, Tu W, Murray MD. Patient perception and provider assessment of severity of heart failure as predictors of hospitalization. Heart Lung 2005 March;34(2):89–98.
[36] Havranek EP, McGovern KM, Weinberger J, Brocato A, Lowes BD, Abraham WT. Patient preferences for heart failure treatment: utilities are valid measures of health-related quality of life in heart failure. J Card Fail 1999 June;5(2):85–91.
[37] Lewis EF, Lamas GA, O'Meara E, et al. Characterization of health-related quality of life in heart failure patients with preserved versus low ejection fraction in CHARM. Eur J Heart Fail 2007 January;9(1):83–91.
[38] Rector TS. A conceptual model of quality of life in relation to heart failure. J Card Fail 2005 April;11(3):173–6.
[39] Coats AJ. Ethical authorship and publishing. Int J Cardiol 2009;131:149–50.