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Research paper

Predictors and outcomes of quality of life in elderly patients with heart failure

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ABSTRACT

Study objective: This study aims to identify predictors of health related quality of life (HRQoL) among patients with heart failure (HF) and assess whether HRQoL was a predictor of rehospitalisation and mortality, and if age influenced the findings.

Design: Observational cohort study.

Setting: Seven hospitals in the Northern Sydney Local Health District, Sydney, Australia.

Participants: Community dwelling patients who completed a Minnesota Living with HF questionnaire (MLHFQ) within 30 days of discharge after a HF hospitalisation.

Main outcome measure: Multivariable linear regression models were used to identify predictors of MLHFQ scores (higher score = worse HRQoL) and adjusted Cox regression models to assess the impact of MLHFQ scores on one-year rehospitalisation and mortality. Separate analyses were conducted for those aged ≤ 80 or >80 years.

Results: 1911 patients of mean age 79 years (57 % aged >80 years) were included in this analysis. Among those aged ≤ 80 years; younger age, lower haemoglobin and presenting symptoms at hospitalisation of exertional dyspnoea, peripheral oedema and fatigue were predictors of worse post-discharge MLHFQ scores. In patients aged >80 years, living alone, chronic kidney disease, exertional dyspnoea and peripheral oedema were predictors of worse MLHFQ scores. Worse MLHFQ scores predicted one-year HF readmissions in those aged >80 years (HR 1.22, 95 % CI 1.07–1.37) but not those aged ≤ 80 years (HR 0.90 95 % CI 0.71–1.10).

Conclusions: In-hospital predictors can be identified for worse HRQoL post-discharge for HF. These vary according to age, and should be addressed prior to discharge.

1. Introduction

Heart failure (HF) is associated with high morbidity and mortality and reduced quality of life [1,2]. Health related quality of life (HRQoL) measures are important tools to assess for how an individual's health affects their quality of life (QoL) they have been shown to predict important clinical outcomes including rehospitalisation and mortality [3–6]. The impact of HF on HRQoL appears to be greater than many other chronic cardiac and non-cardiac diseases [7]. The determinants of HRQoL in HF are less well understood, particularly in the elderly. For instance one study of HF patients aged >65 years found that age, sex, diabetes and respiratory diseases predicted some dimensions of HRQoL but not others [8]. A second study of HF patients aged >65 years found

that higher NYHA class, lower income, and longer duration of HF were independent predictors of worse HRQoL [9]. However, factors are inconsistent, so that in another study of 542 HF patients aged >60 years in a primary care setting female sex, higher NYHA class, depression, low socioeconomic class, comorbid disease and older age to be associated with worse HRQoL [10]. There has also been suggestion that chronic HF appears to have lesser impact on HRQoL in older patients compared to their younger counterparts [11,12]. To our knowledge no prior study has assessed the impact of recent hospitalisation features such as presenting symptoms, precipitants and laboratory investigations on HRQoL. Other unknowns include whether determinants of HRQoL differ between younger and older patients with HF, and whether the impact of HRQoL on clinical outcomes differs in an elderly population.

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Table 1
Baseline patient characteristics according to quartile of Minnesota Living with Heart Failure Questionnaire score.

	Quartile 1 0–25	Quartile 2 26–45	Quartile 3 46–62	Quartile 4 63–105	p-Value for trend
Number of patients	496	487	455	473	
Patient demographics					
Age, years (SD)	81 (9)	80 (9)	79 (11)	77 (12)	<0.001
Age >80 years, n (%)	315 (64)	291 (60)	250 (55)	228 (48)	<0.001
Male sex, n (%)	251 (51)	282 (58)	257 (57)	258 (55)	0.327
Lives alone, n (%)	193 (39)	192 (40)	154 (34)	119 (26)	<0.001
Single (unmarried or widowed), n (%)	45 (9)	45 (9)	36 (8)	39 (8)	0.461
Speaks English at home, n (%)	458 (93)	454 (94)	434 (96)	435 (93)	0.907
Born in Australia, n (%)	275 (55)	288 (59)	280 (62)	276 (58)	0.187
Has private insurance, n (%)	245 (50)	206 (43)	187 (42)	211 (46)	0.104
Medical history					
HFpEF (LVEF \geq 50 %), n (%)	154 (34)	162 (36)	152 (37)	172 (39)	0.146
Atrial fibrillation, n (%)	53 (11)	61 (13)	56 (12)	54 (11)	0.426
Hypercholesterolaemia, n (%)	182 (38)	178 (38)	155 (36)	158 (35)	0.425
Chronic kidney disease, n (%)	54 (11)	69 (15)	74 (17)	81 (18)	0.001
Diabetes, n (%)	108 (22)	111 (23)	112 (26)	126 (28)	0.042
Hypertension, n (%)	311 (64)	277 (58)	279 (65)	276 (62)	0.311
Ischemic heart disease, n (%)	263 (54)	256 (54)	254 (59)	234 (52)	0.844
Current smoker, n (%)	23 (5)	13 (3)	18 (4)	21 (5)	0.924

HFpEF, heart failure with preserved ejection fraction; LVEF, Left ventricular ejection fraction. All numbers are expressed as means and standard deviation unless otherwise specified.

Given the aging population, the prevalence of HF will continue to rise, particularly in the very elderly group aged over 80 years. It is estimated that 12 % of Americans aged over 80 years and 16 % of Europeans aged over 80 years have HF [13,14]. The Management of Cardiac Failure (MACARF) program includes a particularly elderly group of patients, and is a unique dataset to gain better understanding predictors of QoL among very elderly patients with HF. This is particularly important since management priorities in this patient group focus more on maintaining QoL and minimizing time in hospital rather than reducing mortality. Indeed most patients with HF value QoL as more important than prolonged survival [15,16]. This study aims to 1) identify predictors of HRQoL in HF, 2) assess whether HRQoL was a predictor of rehospitalisation and mortality, and 3) determine whether these findings differ according to age.

2. Methods

2.1. Study population

This study was an analysis of data collected prospectively from patients hospitalised with a primary diagnosis of HF between November 1998 and June 2019. HF was diagnosed using the Framingham criteria [17] and all patients >18 years were offered a referral to the program. The study included seven hospitals in the Northern Sydney Area Health District, Australia, who were enrolled in the MACARF program. The program aims to reduce the burden of HF by offering home visits, patient education and follow-up phone calls from HF specialist nurses. Funding of the program and database was through the Northern Sydney Local Health District (G. Tofler, Medical Director of MACARF).

In the present analysis, we included patients who survived their index HF hospitalisation, and subsequently had a HF nurse follow-up home visit and completed a Minnesota living with heart failure questionnaire (MLHFQ) within 30 days of discharge. The MLHFQ questionnaire was conducted by the HF nurse at the time of the home visit. The MLHFQ is a self-administered disease-specific questionnaire for patients with HF, comprising 21 items rated on six-point Likert scales, representing different degrees of impact of HF on HRQoL, from 0 (none) to 5 (very much) [18]. It provides a total score (range 0–105, from best to worst HRQoL), as well as scores for two dimensions, physical (8 items, range 0–40) and emotional (5 items, range 0–25). The other eight items (of the total of 21) are only considered for the calculation of the total score. A higher MLHFQ score indicates greater impairment and worse

QoL. The MLHFQ has been validated in community dwelling patients with HF [19].

Recorded data included sociodemographic, risk factors, comorbid diseases and hospitalisation details including presenting symptoms, precipitants of HF hospitalisation, hospital length of stay, laboratory results and left ventricular ejection fraction on transthoracic echocardiogram. Presenting symptoms were reported by the patients to dedicated HF nurses, who recorded the data. Precipitants of HF were determined from a pre-determined list of potential causes of HF decompensation which includes: ischemic heart disease, arrhythmia, medication non compliance, dietary non compliance, medication changes, other precipitants or unknown precipitants. These precipitants were identified by the treating medical team, and more than one precipitant could be attributed to a single hospitalisation. Readmissions were differentiated based on whether the primary cause was a HF exacerbation or non-HF. All patients were followed up for subsequent readmissions and death. Readmissions were recorded if the patients were rehospitalised in the seven participating hospitals within the Northern Sydney Local Health District, Australia. Ischemic heart disease and chronic kidney disease were noted if they were mentioned as a prior diagnosis in the medical records. Data were recorded into a database by dedicated HF nurses.

2.2. Study outcomes

Outcomes of interest included 1-year hospital rehospitalisation due to HF or non-HF causes, and all-cause mortality. If a patient suffered the outcome of interest prior to their 30 day follow-up home visit, they were excluded from analysis for that particular event.

Mortality was documented through a combination of hospital records, follow-up phone calls and death notices.

2.3. Statistical analysis

Analyses were performed for the entire cohort, and then separately for those patients aged >80 years and \leq 80 years. Age 80 years was chosen because it was close to the average age of the total cohort (79 years). Categorical data were summarized as counts and percentages, and continuous data were expressed as either mean (SD) or median (interquartile range). Tests for linear trends in MLHFQ scores according to baseline and hospitalisation characteristics were assessed by including MLHFQ score as a continuous variable in a linear regression

Table 2
Hospitalisation details according to quartile of Minnesota Living with Heart Failure Questionnaire score.

	Quartile 1 0–25	Quartile 2 26–45	Quartile 3 46–62	Quartile 4 63–105	p-Value for trend
Presenting symptoms					
Exertional dyspnoea, n (%)	412 (88)	435 (92)	406 (92)	430 (95)	<0.001
Paroxysmal nocturnal dyspnoea, n (%)	116 (25)	149 (32)	148 (34)	175 (39)	<0.001
Cough, n (%)	127 (27)	153 (33)	119 (27)	128 (28)	0.991
Fatigue, n (%)	140 (30)	189 (40)	187 (42)	198 (44)	<0.001
Needing to take more rest during daytime, n (%)	80 (17)	109 (23)	124 (28)	119 (26)	<0.001
Weight gain, n (%)	44 (9)	65 (14)	73 (17)	79 (18)	<0.001
Peripheral oedema, n (%)	169 (36)	230 (49)	237 (54)	264 (59)	<0.001
Anorexia, n (%)	61 (13)	77 (16)	94 (21)	89 (20)	<0.001
Palpitations, n (%)	50 (11)	47 (10)	57 (13)	63 (14)	0.020
Chest discomfort, n (%)	72 (15)	91 (19)	91 (21)	80 (18)	0.390
Precipitant of admission, n (%)					
Ischemic heart disease, n (%)	124 (26)	110 (23)	130 (29)	141 (30)	0.095
Arrhythmia, n (%)	135 (28)	121 (25)	141 (32)	140 (30)	0.126
Medication non-compliance, n (%)	32 (7)	27 (6)	39 (9)	26 (6)	0.988
Infection, n (%)	122 (25)	133 (28)	115 (26)	120 (26)	0.775
Dietary non-compliance, n (%)	38 (8)	45 (9)	43 (10)	43 (9)	0.785
Medication adverse effect, n (%)	12 (3)	8 (2)	19 (4)	15 (3)	0.064
Change in medication, n (%)	34 (7)	36 (8)	30 (7)	35 (8)	0.929
Other precipitant, n (%)	25 (5)	30 (6)	37 (8)	43 (9)	0.015
Unknown precipitant, n (%)	96 (20)	113 (24)	82 (19)	93 (20)	0.724
Investigations					
Length of hospital stay ≥ 7 days, n (%)	183 (37)	204 (42)	206 (45)	214 (45)	0.005
Serum sodium, mmol/L (SD)	139 (4)	138 (4)	138 (5)	138 (5)	0.173
Serum potassium, mmol/L (SD)	4.3 (0.5)	4.4 (0.6)	4.3 (0.6)	4.3 (0.5)	0.808
Serum creatinine, mmol/L (SD)	118 (60)	121 (58)	123 (58)	120 (64)	0.613
Serum albumin, g/L (SD)	37 (5)	36 (5)	37 (5)	37 (4)	0.413
Serum haemoglobin, g/L (SD)	128 (18)	124 (19)	126 (19)	125 (18)	0.354
Left ventricular ejection fraction, percent (SD)	40 (16)	41 (16)	42 (16)	42 (17)	0.425

All numbers are expressed as means and standard deviation unless otherwise specified.

model. The relationships between physical and emotional MLHFQ scores were assessed with scatter plots and Pearson correlation coefficients. All univariate variables with p values < 0.05 were considered for the multivariate linear regression. Collinearity (defined as $R \geq 0.50$) was checked between relevant variables, and only 1 of the 2 variables

was entered into the final model if demonstrated. For certain variables that were closely correlated we included one variable only – we included exertional dyspnoea but not paroxysmal nocturnal dyspnoea; fatigue over needing to take more rest; peripheral oedema over weight gain and living alone over single marital status. Separate models were constructed for the overall score and the two dimensions, physical and emotional. Missing data were dealt with using a pair-wise analysis.

The associations of physical, emotional and overall MLHFQ scores to first occurrence of each study outcome were estimated using Hazard Ratios (HR) and 95 % CIs derived from Cox proportional regression models. HRs for QoL score was estimated per 1-SD increase. The models were adjusted for age, sex, living alone, left ventricular ejection fraction, hospital length of stay and comorbidities at baseline including atrial fibrillation, ischemic heart disease, hypertension, diabetes, smoking status and chronic kidney disease. Separate models were constructed for physical, emotional and overall MLHFQ scores because these measures were highly correlated. A linear trend across quarters of MLHFQ scores was tested taking the quartiles as a continuous variable ranging from 1 to 4. All analyses used $p < 0.05$.

3. Results

There was a total of 7845 patients registered in the MACARF database from November 1998 and June 2019, of which a total of 1911 patients completed a MLHFQ at a follow-up home visit within 30 days of discharge. The mean (SD) total MLHFQ score was 44.0 (24.0), mean (SD) physical MLHFQ score was 22.8 (11.2) and mean (SD) emotional MLHFQ score was 9.0 (7.2). Physical scores were significantly correlated with emotional scores ($R = 0.58$, $p < 0.001$) (Supplemental Fig. 1). The mean (SD) age of the population was 79 [11] years, and younger patients had higher overall MLHFQ scores (worse QoL) (Table 1). Patients with higher overall MLHFQ scores were less likely to live alone, had a greater prevalence of chronic kidney disease and diabetes and had a longer length of hospital stay for the index HF admission (Table 2). Patients with higher proportions of presenting symptoms for their index admission had higher overall MLHFQ scores (Table 2). The baseline characteristics of patients aged ≤ 80 years and > 80 years according to quartiles/quarters of MLHFQ scores are shown in Supplementary Tables 1–4.

3.1. Predictors of HRQoL

Among the entire cohort, older age and living alone was associated with lower overall, physical and emotional MLHFQ scores (Supplemental Table 5). Meanwhile, chronic kidney disease, exertional dyspnoea, fatigue and peripheral oedema were predictors of higher overall MLHFQ scores.

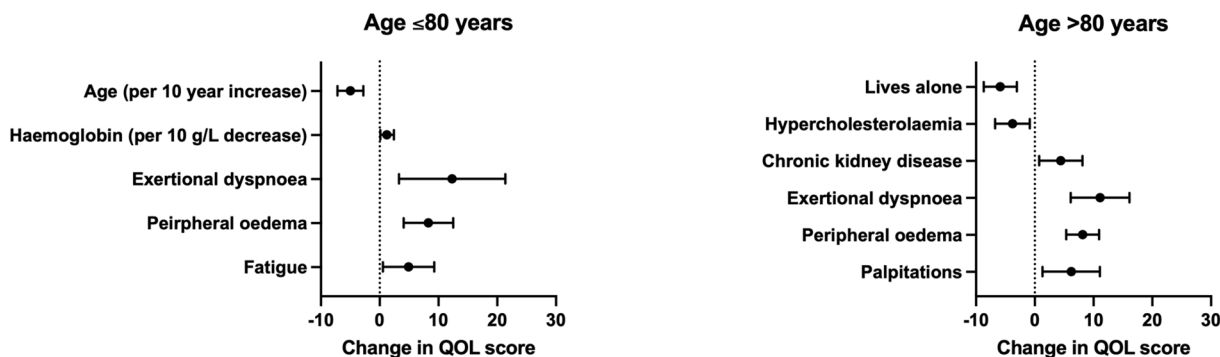
Among patients aged ≤ 80 years, younger age was associated with higher overall, physical and emotional MLHFQ scores (Fig. 1). A lower haemoglobin was associated with higher overall and physical but not emotional MLHFQ scores. Exertional dyspnoea and peripheral oedema were also predictors of overall and physical but not emotional MLHFQ scores whereas fatigue was a predictor of overall and emotional but not physical MLHFQ scores (Fig. 1).

Among patients aged > 80 years, those who lived alone had lower overall, physical and emotional MLHFQ scores (Fig. 1). Chronic kidney disease was associated with higher overall and emotional MLHFQ scores. Exertional dyspnoea, peripheral oedema and palpitations were predictors of higher overall, physical and emotional MLHFQ scores (Fig. 1).

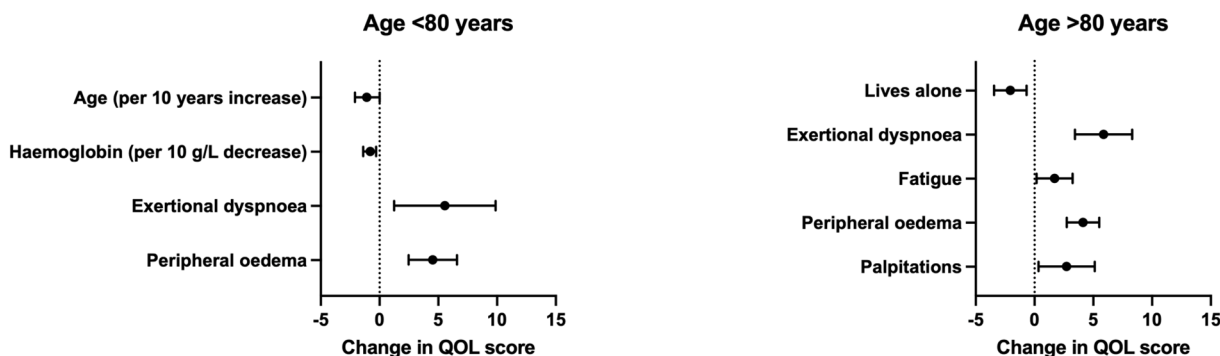
3.2. Effect of HRQoL scores on readmission and death

In those patients aged ≤ 80 years, MLHFQ scores were not independent predictors of one year all-cause, HF and non-HF readmissions (Table 3). There was a trend for higher mortality rates in those patients

Total QoL



Physical QoL



Emotional QoL

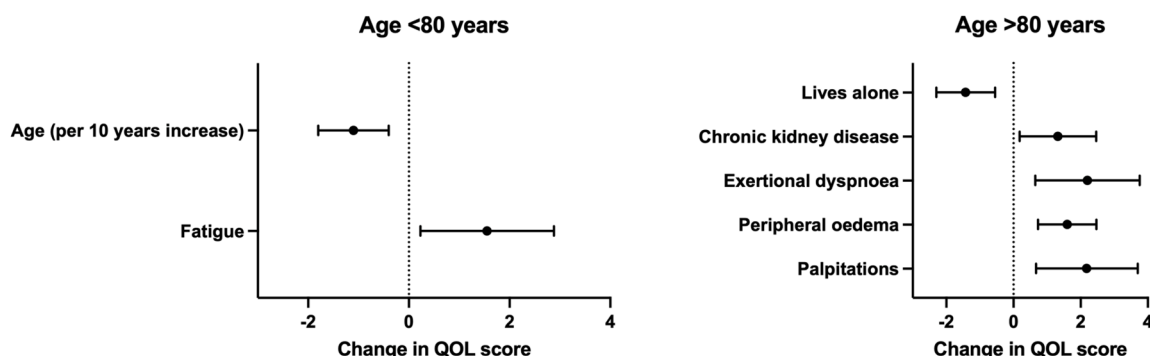


Fig. 1. Independent predictors of Minnesota Living with Heart Failure Questionnaire score in patients aged less than and older than 80 years. Predictors identified by including those variables with $p < 0.05$ in univariate analysis into a multivariate linear regression. r variables included in the multivariate model for age ≤ 80 years were chronic kidney disease, left ventricular ejection fraction, dietary non-compliance, and other precipitants of the index hospitalisation. Other variables included in the multivariate model for age >80 years model were fatigue and anorexia as presenting symptoms of index hospitalisation and arrhythmia and dietary non-compliance as precipitants of index hospitalisation.

with higher overall MLHFQ scores (HR 1.14, 95 % CI 1.00–1.29). Among those patients aged >80 years, higher overall MLHFQ scores were predictive of one-year HF readmissions (HR 1.22, 95 % CI 1.07–1.37) and all-cause readmissions (HR 1.10, 95 % CI 1.01–1.21) but not non-HF readmissions (HR 1.03, 95 % CI 0.92–1.14) (Table 3). The risk of 1 year HF readmissions increased log-linearly with increasing overall MLHFQ scores in those aged >80 years ($p = 0.008$) (Fig. 2).

4. Discussion

In this study of community dwelling HF patients who had a recent HF hospitalisation, worse HRQoL scores were independent predictors of HF readmissions in those patients aged >80 years but not those aged ≤ 80 years. Presenting symptoms at the time of HF hospitalisation were significant predictors of worse HRQoL post-discharge. These findings reinforce the importance of identifying and adequately addressing

Table 3
Association of Minnesota Living with Heart Failure Questionnaire score with clinical outcomes in patients aged ≤80 years and >80 years.

Total population	Events/Total	HR (95 % CI)	p-Value
One year readmission	738/1679	1.05 (0.98, 1.12)	0.164
One year HF readmission	294/1682	1.10 (0.98, 1.22)	0.092
One year non-HF readmission	577/1680	1.01 (0.92, 1.10)	0.873
One year mortality	202/1683	1.14 (1.00, 1.29)	0.056

Age ≤80 years	Events/total	HR (95 % CI)	p-Value
One year readmission	281/731	0.99 (0.86, 1.10)	0.807
One year HF readmission	110/733	0.90 (0.71, 1.10)	0.314
One year non-HF readmission	219/732	1.00 (0.86, 1.12)	0.970
One year mortality	59/734	1.26 (0.99, 1.54)	0.063

Age >80 years	Events/total	HR (95 % CI)	p-Value
One year any readmission	457/948	1.10 (1.01, 1.21)	0.032
One year HF readmission	184/949	1.22 (1.07, 1.37)	0.004
One year non-HF readmission	358/948	1.03 (0.92, 1.14)	0.612
One year mortality	143/949	1.09 (0.93, 1.26)	0.280

Cox models adjusted for age, sex, living status, left ventricular ejection fraction, hospital length of stay and comorbidities including atrial fibrillation, ischemic heart disease, hypertension, diabetes, smoking status and chronic kidney disease. HF, heart failure.

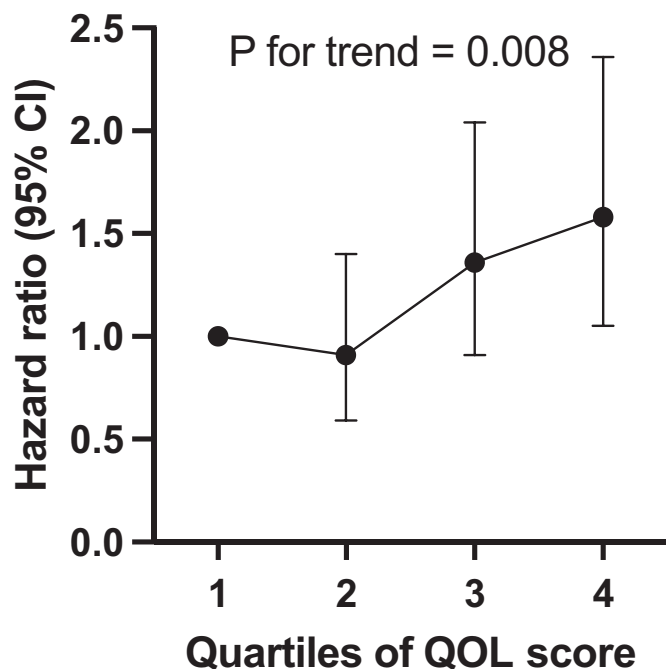


Fig. 2. Association of overall Minnesota Living with Heart Failure Questionnaire score with 1-year HF hospitalisation in patients aged >80 years. Cox models were adjusted for age, sex, living status, left ventricular ejection fraction, hospital length of stay and comorbidities including atrial fibrillation, ischemic heart disease, hypertension, diabetes, smoking status and chronic kidney disease.

patient symptoms as a key strategy for improving HRQoL and preventing HF rehospitalisation in the elderly. HRQoL assessments should also form part of longitudinal care for all patients with HF, but particularly the elderly, where the goals are often to minimize rehospitalisation.

In the management of HF, clinicians focus on patient comorbidities, investigation results and hospital length of stay as markers of worse clinical outcomes. In our study, patient symptoms at the time of HF

hospitalisation were a significant determinant of HRQoL in the community during the home visit up to 30 days after hospital discharge. It is likely that the patients' symptoms were not adequately controlled at the time of hospital discharge and contributed to not only worse QoL in the community, but also higher risk of subsequent HF readmission. Indeed HF patients are frequently readmitted for the same precipitants of their initial HF admission [20]. Clinicians should be reminded to routinely identify and address their patients' presenting symptoms during each HF hospitalisation and have a targeted management for these symptoms in the community. For example, patients with ischemic precipitants of HF should have their angina appropriately treated, whether through medical therapy or revascularisation [21].

Prior studies have shown that worse HRQoL is associated with increased risk of rehospitalisation and mortality in patients with HF [3–6,22–24]. The link between worse HRQoL scores and all-cause death and clinical outcomes appears to be independent of the severity of HF and traditional markers of a patient's HF severity [24]. Our study assessed whether hospitalisation characteristics are able to predict HRQoL in the community. We found that presenting symptoms at the time of hospitalisation, in particular exertional dyspnoea and peripheral oedema, were significant determinants of HRQoL after discharge. Prior studies have identified NYHA class, a marker of dyspnoea and congestion, as a predictor of worse HRQoL, but these studies acknowledge that NYHA class is unlikely to capture all elements of HRQoL for each individual [1,24].

Our findings reinforce the importance of treating congestion, with clinicians ideally ensuring that patients are euvoletic at the time of discharge, and receive close monitoring in the community for signs and symptoms of congestion. With bed limitations and financial constraints increasing the pressure to discharge patients after a short length of hospital stay, the minimization of congestive symptoms post-discharge is particularly important. We found that chronic kidney disease was a predictor of worse HRQoL, which may be related to symptoms such as fatigue, pain and pruritis [25]. However, it may also be related to worsening congestion in those patients with concomitant kidney disease and HF, who often require cautious balance of diuretic dose to achieve effective diuresis while avoiding renal deterioration [26].

Optimising treatment of non-congestive symptoms is also important to improve HRQoL. In our study, palpitations and fatigue were also important contributors to HRQoL and may be helped by specific interventions. For example, maintaining sinus rhythm in HF patients with atrial fibrillation through medication or ablation procedures can improve HRQoL [27,28]. Similarly, iron deficiency is associated with worse HRQoL in HF, and intravenous iron administration can improve 6-minute walk distance and HRQoL [29–31]. Addressing depression with both non-pharmacological and pharmacological approaches may improve HRQoL in HF patients, and depression should be regularly screened and treated when appropriate [32–34].

Our finding that younger age was a predictor of worse HRQoL, has been observed in prior studies [35,36]. The mechanisms underlying this remain unclear but are likely influenced by the mismatch between reality and expectations. Early referral of patients with HF to supportive/palliative care for adequate symptom control may not only improve QoL but also prevent HF readmission. A prior study of patients with acute HF found that that inpatient palliative care involvement was associated with improved symptom burden and QoL [37]. Interestingly, we found that living alone was associated with better HRQoL in the elderly, both in terms of physical, emotional and total QoL outcomes. This finding may be related to the importance of the elderly maintaining their independence on perceived QoL, particularly given we did not find any significant association between being single and HRQoL. The ability to live alone may also represent a higher level of functioning or resilience.

Current HF guidelines recommend therapies that have proven efficacy in reducing mortality and hospitalisation [38,39]. Several of these therapies are associated with improved HRQoL including angiotensin receptor blocker/neprolsins inhibitors [40] in HF rEF and sodium-

glucose Cotransporter-2 (SGLT2) inhibitors in both HFpEF and HFrEF [41]. Exercise programs can also improve HRQoL in addition to increasing exercise capacity [42,43]. Future trials should continue to investigate the impact of novel therapies on quality of life and assess the role of HRQoL as a surrogate for clinical outcomes.

There are several limitations to discuss. Firstly, our patient population was not a random sample of HF patients. Nevertheless, all patients with HF admitted to hospital were screened for enrolment and patients were excluded only if they refused. Secondly, patients received patient education, phone calls and home visits from specialist nurses. Thirdly, HF signs at the post discharge visit were not included in this analysis. This was an observational study, with some incomplete data collection. Besides certain laboratory data such as serum albumin (33 %) and haemoglobin levels (21 %), rates of missing data in our dataset was low (<5 %). Rehospitalisations that occurred outside our health district may not have been recorded. Finally, we did not have data on MLHFQ scores at baseline, nor at the time of hospitalisation, and so we could not provide insights into predictors of change in HRQoL metrics.

In conclusion, reduced HRQoL on a follow-up home visit up to 30 days post discharge was associated with increased HF hospitalisation in patients aged >80 years. There are some differences in predictors of HRQoL based on patient age less than or >80 years, however presenting symptoms at the time of HF hospitalisation were important determinants of the HRQoL post discharge in the community in both age groups. These symptoms should be routinely identified and optimally treated with seamless linkage from the hospital to the community.

CRedit authorship contribution statement

Nelson Wang: Conceptualization, Writing – original draft, Formal analysis, Validation, Methodology. **Susan Hales:** Data curation, Writing – review & editing. **Robyn Gallagher:** Data curation, Writing – review & editing, Supervision. **Geoffrey Tofler:** Conceptualization, Methodology, Resources, Writing – review & editing, Supervision, Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ahjo.2022.100188>.

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