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RESEARCH ARTICLE

Quality of life assessed 6 months after hospitalisation for acute heart failure: an analysis from REPORT-HF (international REgistry to assess medical Practice with lOngitudinal obseRvation for Treatment of Heart Failure)

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Aims Recovery of well-being after hospitalisation for acute heart failure (AHF) is a measure of the success of interventions and the quality of care but has rarely been quantified. Accordingly, we measured health status after discharge in an international registry (REPORT-HF) of AHF.

Methods and results The analysis included 4606 patients with AHF who survived to hospital discharge, had known vital status at 6 months, and were enrolled in the United States of America, Russian Federation, or Western Europe, where the Kansas City Cardiomyopathy Questionnaire (KCCQ) was administered. Median age was 69 years (quartiles 59–78), 40% were women, and 34% had a left ventricular ejection fraction (LVEF) <40%, and 12% patients died by 6 months. Of 2475 patients with a follow-up KCCQ, 28% were 'alive and well' (KCCQ >75), while 43% had poor health status (KCCQ ≤50). Being 'alive and well' was associated with new-onset AHF, LVEF <40%, younger age, higher baseline KCCQ, country, and race. Associations were similar for increasing health status, with the exception of country and addition of comorbidities.

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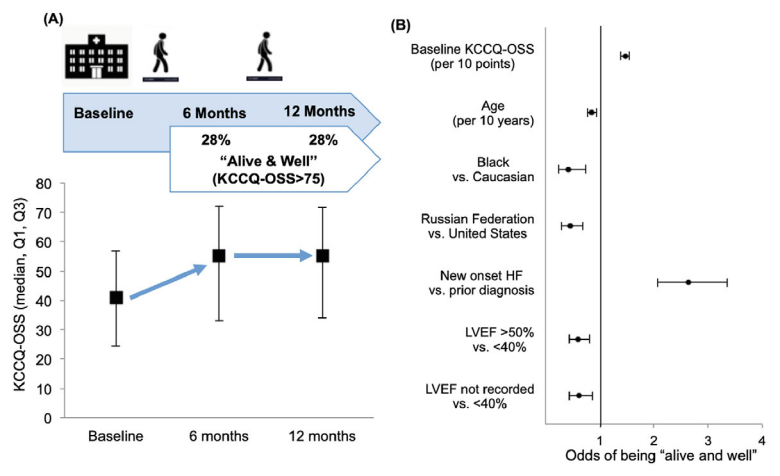
Conclusion In this international global registry, health status recovery after AHF hospitalisation was highly variable. Those with the best health status at 6 months were younger, had new-onset heart failure, and higher baseline KCCQ; nearly one-third of survivors were 'alive and well'. Investigating reasons for changes in KCCQ after hospitalisation might identify new therapeutic targets to improve patient-centred outcomes.

Graphical Abstract



(*A*) Kansas City Cardiomyopathy Questionnaire overall summary score (KCCQ-OSS) at baseline, 6 months, and 12 months. (*B*) Forest plot of characteristics associated with being 'alive and well' at follow-up. LVEF, left ventricular ejection fraction; HF, heart failure. *Multivariable logistic regression.

Keywords Acute heart failure • Kansas City Cardiomyopathy Questionnaire • Post-discharge health status

Introduction

Many patients with heart failure report that well-being is at least as important as prognosis,[1] and there is a move by the American College of Cardiology/American Heart Association to include patient health status for the assessment of quality of heart failure care.[2] Although rates of rehospitalisation and death for patients with acute heart failure (AHF) are well documented, less is known regarding patient-reported outcomes and wellbeing in the months after discharge or features associated with persistence or recovery of impaired quality of life.[3–6]

The international REgistry to assess medical Practice with lOngitudinal obseRvation for Treatment of Heart Failure (REPORT-HF) is a global registry of patients with AHF prospectively enrolled during hospitalisation for incident or decompensated AHF that, unlike clinical trials, had few exclusion criteria.[7–9] In five countries (Germany, Great Britain, the Russian Federation, Spain and the United States of America [USA]), investigators were asked to invite participants to complete the Kansas City Cardiomyopathy Questionnaire (KCCQ) to assess their health status before discharge and at 6 and 12 months after hospital discharge. This provided an opportunity to investigate the natural history and features associated with favourable health status following hospitalisation for AHF in a diverse patient cohort enrolled in several world regions.

Methods

This study was performed in accordance with the principles outlined in the Declaration of Helsinki. Locally appointed ethics committees approved the research protocol, and informed consent was obtained from the participants or their guardians.

Methods for screening, enrolment, data collection, and follow-up of participants have been described previously.[7] Any patient ≥18 years old hospitalised with a primary diagnosis of AHF as determined by the treating clinician was eligible, except those involved in a therapeutic trial or unable or unwilling to provide informed consent. Patients were enrolled between July 2014 and March 2017. Data were recorded using the same case report form across all sites. Patients were

managed according to local clinical practice. Vital status was assessed by enrolment sites and, where available, reporting databases.

Participants enrolled in Germany, Great Britain, Spain, the USA, and the Russian Federation were invited to complete the KCCQ in their preferred language before hospital discharge (baseline) and at 6- and 12-month study follow-up. The primary analysis was based on participants who completed the KCCQ or had died within 6 months of hospital discharge; outcomes at 12 months were used if the 6-month follow-up was missing. Six rather than 12 months was chosen for the primary analysis because the data were more complete and there were fewer deaths at this time.

The KCCQ is a 23-item, patient-reported, disease-specific health status measure quantifying multiple health domains, including symptoms, physical and social functioning, and quality of life. The overall summary score (KCCQ-OSS) averages these four domains to provide a more holistic description of health status.[10] Scores range from 0–100, with higher scores indicating better function, fewer symptoms and better health status. The KCCQ has been shown to be a valid, reproducible and sensitive measure of patients' health status and is associated with mortality, hospitalisation rates and costs,[9,11,12] and it has been approved by the US Food and Drug Administration as a clinical outcome assessment.[13] A mean difference of 5 points is considered clinically important.[14] For this analysis, patients who were alive and reported a KCCQ-OSS >75 at 6 months were considered to be 'alive and well', that is, alive and with excellent health status.[11,15–17]

Statistical analyses

Patient demographics, comorbidities, hospital discharge medications, and region are described as percentages; continuous variables are described by medians and first and third quartiles. The distribution of the KCCQ-OSS and sub-scales at enrolment and each follow-up are reported. Logistic regression models were used to examine associations between patient factors and country with the primary outcome of being 'alive and well' (i.e. alive and excellent health status, with KCCQ-OSS > 75) at 6 months. Univariate, baseline-adjusted (i.e. adjusted for enrolment KCCQ-OSS), and multivariable models were constructed. The following were included in multivariable models based on prior knowledge: enrolment KCCQ-OSS if available (per 10 points; also included in the baseline-adjusted model); age (per 10 years), sex (male, female), race (Black, Asian, or other vs. White); smoking status (former, current vs. never); index hospitalisation for decompensation of chronic heart failure (yes, no); left ventricular ejection fraction (LVEF; <40% vs. 40%–49%, ≥50%, and not recorded); history of hypertension, atrial fibrillation, diabetes, chronic kidney disease, coronary artery disease (defined as having a history of coronary artery bypass, percutaneous coronary intervention, acute coronary syndrome, or myocardial infarction); cause of heart failure (HF) (ischaemic vs. hypertensive, cardiomyopathy, valvular, other, and unknown).

Similarly, univariate, baseline-adjusted, and multivariable linear regression models were constructed to explore relationships with continuous post-discharge KCCQ-OSS among the patients who had completed a 6-month or 12-month KCCQ-OSS. In sensitivity analyses, missing enrolment data were imputed using predictive mean matching within the 'mice' package R (v3.12.10), and separate models were constructed and weighted by the inverse of the predicted probability of having KCCQ-OSS data available at follow-up, derived from a non-parsimonious model for being followed up. Post-hoc multivariable logistic and linear regression models were performed, stratified by ejection fraction. Findings were considered significant at $p < 0.05$, with 2-tailed testing. Analyses were conducted in R (v3.6.0) using the 'rms' package. Multivariable logistic regression model fit assessed by the le Cessie–van Houwelingen normal test statistic for the unweighted sum of squared errors revealed no evidence for lack of fit.[18] Multivariable linear regression model fit assessed by quantile-quantile plot of residuals was also deemed sufficient.

Results

The main findings are summarized visually in the *Graphical Abstract*.

Baseline characteristics

Of 4804 patients enrolled in the five participating countries (*Figure 1*), 4685 survived to hospital discharge, and a further 4606 also had known vital status at 6 months and are therefore the focus of these analyses. In total, 563 (12%) died within 6 months, with post-discharge mortality ranging from 9% in Russia and Spain to 15% in Great Britain. At follow-up, 2475 individuals were alive and had KCCQ-OSS available, including 2200 with 6-month KCCQ-OSS available and 275 with only a 12-month KCCQ-OSS available (these two groups were combined). A further 1568 were alive but had not completed a KCCQ-OSS. Overall, 982 (21%) were enrolled in Germany, 564 (12%) in Great Britain, 1201 (26%) in the Russian Federation, 567 (12%) in Spain, and 1292 (28%) in the USA. Median (Q1, Q3) age was 69 (59, 78) years, 40% were women, 82% were Caucasian, 34% had a LVEF <40% (HF with reduced ejection fraction [HFrEF]) and 42% had coronary

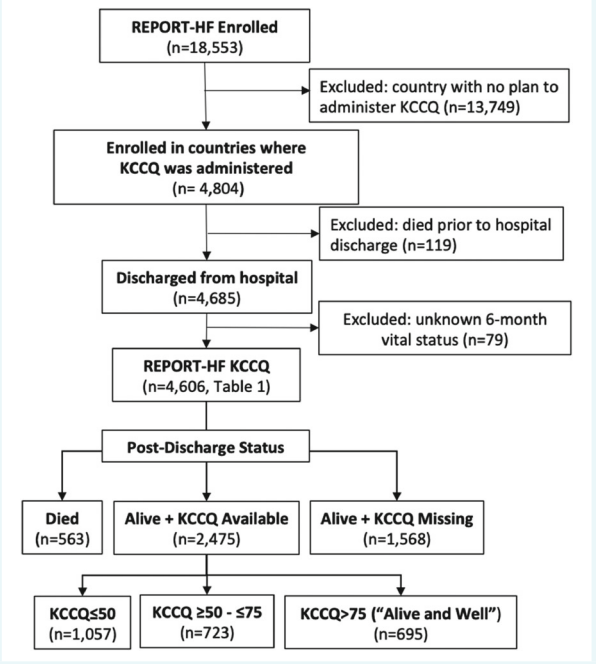


Figure 1 Study flow diagram. KCCQ, Kansas City Cardiomyopathy Questionnaire.

artery disease. At discharge, patients with HFrEF were generally prescribed guideline-recommended pharmacological therapy, including angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEi/ARB) (76%), beta-blocker (87%) and mineralocorticoid receptor antagonists (MRA) (65%). Patients who died within 6 months were less likely to receive such treatments.

Table 1 shows baseline patient-characteristics for the 4606 participants with post-discharge follow-up available, according to 6-month health status. Of these, 695 (28%) were 'alive and well' (KCCQ-OSS >75). However, 1057 (23% overall and 43% of the 2475 with a post-discharge KCCQ) had poor health status (KCCQ-OSS ≤50), and 1620 patients (35% overall and 65% of those with a post-discharge KCCQ) either died or were living with a KCCQ-OSS ≤50. In these unadjusted comparisons, participants who were 'alive and well' at 6 months (KCCQ >75) had better baseline KCCQ-OSS (median 56), were younger (median age 66 years), more likely to be men (72%), had fewer comorbid conditions including coronary artery disease, were more likely to have new-onset HF (49%), and more likely to have HFrEF (44%). In contrast, those who died within 6 months had a lower baseline KCCQ-OSS (median 33), were older (median age 74 years), were more likely to be Black, had more comorbid conditions, and less often had new-onset HF (19%). Patients who died also had lower blood pressure, estimated glomerular filtration rate, and fewer were prescribed an ACEi or ARB, beta-blocker, or an MRA. Patients who survived but with a KCCQ ≤50 generally had characteristics similar to those who died. Findings were similar when restricted to participants who also had a baseline KCCQ-OSS (online supplementary *Tables S1* and *S2*).

We sought to understand the characteristics of the 1568 discharged patients who were alive at 6 months but did not have a follow-up KCCQ. Of these, baseline KCCQ was available for 420 patients (27%). Patients from the Russian Federation were most likely (93%) and those from the USA least likely (40%) to complete a follow-up KCCQ. Black patients, who were almost entirely enrolled in the USA, were least likely (27%) to complete a follow-up KCCQ. In other respects, patients who survived and did or did not complete a follow-up KCCQ had similar characteristics.

Trajectory of health status after hospital discharge

Most of the improvement in KCCQ-OSS occurred within 6 months with, on average, little further change by 12 months (*Table 2*, *Figure 2*, and online supplementary *Figure S1*). Symptom frequency, burden, physical limitations, total symptom score, and quality of life all improved from baseline to 6 months. Median values after improvement in each domain were consistent with persistent moderate or severe impairment.[12]

Predictors of being 'alive and well' after discharge

In a multivariable logistic model (*Table 3*), better baseline KCCQ, younger age, new-onset HF, and LVEF <40% versus >50% was associated with greater odds of being 'alive and well' at 6 months. The variables with largest magnitude associations were baseline KCCQ (odds ratio [OR] 1.5 per 10 points baseline KCCQ-OSS, 95% confidence interval [CI] 1.4, 1.6) and new-onset HF (OR 2.6, 95% CI 2.1, 3.4). Compared to White race, only Black race was associated with lower odds of being 'alive and well', and patients enrolled in Germany and Spain had greater chance of being 'alive and well' than those in the USA, while those enrolled in the Russian Federation had lower odds. Male sex was associated with better odds of being 'alive and well' in the univariate and baseline-adjusted models (online supplementary *Table S3*) but not in the full multivariable model. Imputation of missing baseline data yielded similar results (online supplementary *Table S4*).

Predictors of better post-discharge health status

Results of multivariable linear regression models were similar, with the notable exceptions of country, which was not associated with better health status, and inclusions of atrial fibrillation, diabetes, and coronary artery disease (*Table 3* and online supplementary *Table S5*). Better post-discharge health status was associated with higher baseline KCCQ, younger age, new-onset HF, and LVEF <40% versus >50%. The largest magnitude associations with better post-discharge KCCQ-OSS were: new-onset HF (8.3 points, 95% CI 6.1, 10.4), higher baseline KCCQ-OSS (4.4 points, per 10 points, 95% CI 4.0, 4.9), and absence of diabetes (3.8 points, 95% CI 1.8, 5.9). Compared to White race, only Black race was associated with worse post-discharge health status: −6.6 (95% CI −11.9, −1.4) points. Male sex was associated with better health status in the univariate and baseline-adjusted models (online supplementary *Table S5*), but not in the multivariable model. Multivariable associations were consistent in sensitivity analyses with imputation using predictive mean matching (online supplementary *Table S6*) and weighting by the inverse of the predicted probability of having a post-discharge KCCQ-OSS (online supplementary *Table S7*).

Sensitivity analyses

Participants missing post-discharge KCCQ were slightly older, more often enrolled in the USA, Black, had chronic kidney disease, and unmeasured LVEF than participants who completed at least one follow-up KCCQ. To address potential differential follow-up, we conducted sensitivity analyses addressing missing data, including weighting to account for different probabilities of following up (online supplementary *Tables S4*, *S6*, and *S7*). These results were essentially unchanged from the main models.

Stratification by left ventricular ejection fraction

In contrast to the main analyses, among participants with baseline LVEF <40% (online supplementary *Table S8.1*) we did not detect associations between health status measured by KCCQ and age, country, race, or comorbid conditions, but there was evidence for associations with HF aetiology or smoking. Otherwise,

Table 1 Baseline characteristics by 6-month health status (KCCQ-OSS)

	All	Dead	Alive, KCCQ ≤25	Alive, KCCQ >25–≤50	Alive, KCCQ >50–≤75	Alive, KCCQ >75	Alive, KCCQ missing	*p*-value
n	4606	563	299	758	723	695	1568	
Baseline KCCQ-OSS, mean (SD)	42 (22)	35 (21)	28 (18)	36 (19)	45 (19)	57 (21)	43 (21)	<0.0001
Missing, n	*1891*	*256*	*58*	*139*	*128*	*162*	*1148*	
Baseline KCCQ-OSS, median (Q1, Q3)	41 (25, 58)	33 (20, 48)	25 (15, 39)	36 (20, 48)	47 (31, 59)	56 (41, 73)	42 (26, 59)	<0.0001
Missing, n	*1891*	*256*	*58*	*139*	*128*	*162*	*1148*	
Age (years), mean (SD)	68 (13)	72 (13)	70 (12)	69 (13)	67 (12)	66 (13)	67 (14)	<0.0001
Female sex, *n* (%)	1859 (40.4)	225 (40.0)	139 (46.5)	333 (43.9)	293 (40.5)	197 (28.3)	672 (42.9)	<0.0001
Race, *n* (%)								<0.0001
Caucasian	3770 (81.8)	452 (80.3)	261 (87.3)	676 (89.2)	664 (91.8)	617 (88.8)	1100 (70.2)	
Black	695 (15.1)	91 (16.2)	27 (9.0)	63 (8.3)	44 (6.1)	51 (7.3)	419 (26.7)	
Asian	40 (0.9)	5 (0.9)	4 (1.3)	7 (0.9)	3 (0.4)	9 (1.3)	12 (0.8)	
Other	101 (2.2)	15 (2.7)	7 (2.3)	12 (1.6)	12 (1.7)	18 (2.6)	37 (2.4)	
Country, *n* (%)								<0.0001
USA	1292 (28.1)	188 (33.4)	58 (19.4)	126 (16.6)	112 (15.5)	141 (20.3)	667 (42.5)	
Russian Federation	1201 (26.1)	111 (19.7)	102 (34.1)	384 (50.7)	341 (47.2)	189 (27.2)	74 (4.7)	
Germany	982 (21.3)	120 (21.3)	62 (20.7)	113 (14.9)	125 (17.3)	183 (26.3)	379 (24.2)	
Spain	567 (12.3)	52 (9.2)	31 (10.4)	50 (6.6)	59 (8.2)	105 (15.1)	270 (17.2)	
Great Britain	564 (12.2)	92 (16.3)	46 (15.4)	85 (11.2)	86 (11.9)	77 (11.1)	178 (11.4)	
New-onset HF, *n* (%)	1385 (30.1)	106 (18.8)	56 (18.7)	158 (20.8)	244 (33.7)	342 (49.2)	479 (30.5)	<0.0001
LVEF, *n* (%)								<0.0001
<40%	1565 (34.0)	194 (34.5)	77 (25.8)	223 (29.4)	225 (31.1)	302 (43.5)	544 (34.7)	
40%–50%	711 (15.4)	80 (14.2)	50 (16.7)	129 (17.0)	112 (15.5)	114 (16.4)	226 (14.4)	
>50%	1219 (26.5)	115 (20.4)	84 (28.1)	247 (32.6)	237 (32.8)	145 (20.9)	391 (24.9)	
Not recorded	1111 (24.1)	174 (30.9)	88 (29.4)	159 (21.0)	149 (20.6)	134 (19.3)	407 (26.0)	
Hypertension, *n* (%)	3476 (75.6)	409 (72.8)	233 (78.2)	589 (77.9)	550 (76.2)	471 (67.8)	1224 (78.1)	<0.0001
Missing, n	*6*	*1*	*1*	*2*	*1*	*0*	*1*	
Atrial fibrillation, *n* (%)	2017 (43.8)	292 (52.0)	152 (51.0)	379 (50.1)	305 (42.2)	259 (37.3)	630 (40.2)	<0.0001
Missing, n	*6*	*1*	*1*	*2*	*1*	*0*	*1*	
Diabetes, *n* (%)								<0.0001
Non-diabetic	2796 (60.7)	339 (60.2)	158 (52.8)	484 (63.9)	462 (64.0)	481 (69.3)	872 (55.6)	
Diabetic	1808 (39.3)	224 (39.8)	141 (47.2)	274 (36.1)	260 (36.0)	213 (30.7)	696 (44.4)	
Missing, n	*2*	*0*	*0*	*0*	*1*	*1*	*0*	
CKD, *n* (%)	1357 (29.5)	210 (37.3)	97 (32.4)	275 (36.3)	175 (24.2)	148 (21.3)	452 (28.8)	<0.0001
Missing, n	*2*	*0*	*0*	*0*	*1*	*1*	*0*	
CAD, *n* (%)	1933 (42.0)	256 (45.6)	157 (52.7)	407 (53.8)	344 (47.6)	231 (33.2)	538 (34.3)	<0.0001
Missing, n	*6*	*1*	*1*	*2*	*1*	*0*	*1*	
HF aetiology, *n* (%)								<0.0001
Ischaemic	1503 (32.6)	198 (35.2)	116 (38.8)	310 (40.9)	281 (38.9)	201 (28.9)	397 (25.3)	
Hypertensive	751 (16.3)	73 (13.0)	47 (15.7)	132 (17.4)	110 (15.2)	90 (12.9)	299 (19.1)	
Cardiomyopathy	720 (15.6)	88 (15.6)	33 (11.0)	93 (12.3)	90 (12.4)	136 (19.6)	280 (17.9)	
Valvular	458 (9.9)	58 (10.3)	29 (9.7)	61 (8.0)	71 (9.8)	91 (13.1)	148 (9.4)	
Other	376 (8.2)	51 (9.1)	23 (7.7)	53 (7.0)	42 (5.8)	56 (8.1)	151 (9.6)	
Unknown	798 (17.3)	95 (16.9)	51 (17.1)	109 (14.4)	129 (17.8)	121 (17.4)	293 (18.7)	
Smoking history, *n* (%)								<0.0001
Never	2057 (44.7)	237 (42.1)	155 (51.8)	405 (53.4)	361 (49.9)	283 (40.7)	616 (39.3)	
Former	713 (15.5)	65 (11.5)	28 (9.4)	98 (12.9)	122 (16.9)	123 (17.7)	277 (17.7)	
Current	1620 (35.2)	232 (41.2)	100 (33.4)	230 (30.3)	224 (31.0)	257 (37.0)	577 (36.8)	
Unknown	216 (4.7)	29 (5.2)	16 (5.4)	25 (3.3)	16 (2.2)	32 (4.6)	98 (6.2)	
Medications in HFrEF (LVEF <40%[b]), *n* (%)								
ACEi or ARB	1182 (75.6)	109 (56.5)	61 (79.2)	191 (85.7)	180 (80.0)	228 (75.5)	413 (75.9)	<0.0001
Missing, n	*1*	*1*	*0*	*0*	*0*	*0*	*0*	
β-blockers	1357 (86.8)	134 (69.4)	70 (90.9)	202 (90.6)	206 (91.6)	264 (87.4)	481 (88.4)	<0.0001
Missing, n	*1*	*1*	*0*	*0*	*0*	*0*	*0*	
MRAs	1023 (65.4)	107 (55.4)	52 (67.5)	158 (70.9)	174 (77.3)	206 (68.2)	326 (59.9)	<0.0001
Missing, n	*1*	*1*	*0*	*0*	*0*	*0*	*0*	
Loop diuretics	1406 (89.9)	174 (90.2)	72 (93.5)	200 (89.7)	209 (92.9)	263 (87.1)	488 (89.7)	0.3307
Missing, n	*1*	*1*	*0*	*0*	*0*	*0*	*0*	
Medications in non-HFrEF (LVEF ≥40% or unknown), *n* (%)								
ACEi or ARB	2032 (66.9)	174 (47.3)	146 (65.8)	389 (72.8)	375 (75.6)	297 (75.6)	651 (63.6)	<0.0001
Missing, n	*4*	*1*	*1*	*1*	*2*	*0*	*0*	
β-blockers	2374 (78.2)	271 (73.6)	174 (78.4)	433 (81.1)	410 (82.7)	315 (80.2)	771 (75.3)	0.0023
Missing, n	*4*	*1*	*0*	*1*	*2*	*0*	*0*	

Table 1 (Continued)

	All	Dead	Alive, KCCQ ≤25	Alive, KCCQ >25–≤50	Alive, KCCQ >50–≤75	Alive, KCCQ >75	Alive, KCCQ missing	*p*-value
MRAs	1338 (44.1)	141 (38.3)	120 (54.1)	304 (56.9)	249 (50.2)	197 (50.1)	327 (31.9)	<0.0001
Missing, n	*4*	*1*	*0*	*1*	*2*	*0*	*0*	
Loop diuretics	2613 (86.0)	337 (91.6)	204 (91.9)	454 (85.0)	408 (82.3)	329 (83.7)	881 (86.0)	0.0002
Missing, n	*4*	*1*	*0*	*1*	*2*	*0*	*0*	
Clinical characteristics, median (Q1, Q3)								
SBP (mmHg)	135 (117, 155)	125 (110, 141)	135 (120, 154)	135 (120, 152)	136 (119, 156)	134 (116, 154)	139 (120, 158)	<0.0001
Missing, n	*511*	*59*	*57*	*95*	*120*	*105*	*75*	
DBP (mmHg)	80 (69, 90)	73 (64, 82)	80 (65, 90)	80 (70, 90)	80 (70, 90)	80 (70, 90)	80 (70, 92)	<0.0001
Missing, n	*513*	*59*	*57*	*95*	*120*	*105*	*77*	
Heart rate (bpm)	85 (72, 101)	85 (72, 100)	80 (70, 95)	85 (72, 100)	84 (72, 100)	85 (70, 106)	87 (74, 103)	0.0109
Missing, n	*532*	*62*	*60*	*94*	*127*	*107*	*82*	
eGFR (ml/min/1.73 m^2)	61 (42, 83)	47 (32, 67)	57 (37, 77)	57 (41, 80)	69 (47, 92)	66 (49, 86)	63 (44, 85)	<0.0001
Missing, n	*1995*	*230*	*179*	*508*	*463*	*323*	*292*	

ACEi, angiotensin-converting enzyme inibitor; ARB, angiotensin receptor blocker; CAD, coronary artery disease; CKD, chronic kidney disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; KCCQ-OSS, Kansas City Cardiomyopathy Questionnaire overall summary score; LVEF, left ventricular ejection fration; MRA, mineralocorticoid receptor antagonist; SBP, systolic blood pressure.
KCCQ categorised into 25-point bands of overall summary score distribution at 6 months.
p-values from ANOVA, Kruskal–Wallis tests or Fisher's exact tests as appropriate.
[a]12-month KCCQ was used for 275 participants for whom 6-month KCCQ was not available.
[b]Medications at hospital discharge. Angiotensin receptor–neprilysin inhibitor ($n = 90$) included in angiotensin receptor II blocker category.

Table 2 Kansas City Cardiomyopathy Questionnaire (KCCQ) domains at baseline, 6 months, and 12 months for those with KCCQ overall summary score recorded at baseline

KCCQ domain	Baseline ($n = 2715$)	6 months ($n = 1792$)	12 months ($n = 1567$)
Physical limitation	41.7 (20.8, 66.7)	50.0 (33.3, 79.2)	50.0 (29.2, 75.0)
Missing, n	*115*	*988*	*1199*
Symptom stability	100.0 (75.0, 100.0)	50.0 (50.0, 75.0)	50.0 (50.0, 75.0)
Missing, n	*37*	*944*	*1160*
Symptom frequency	41.7 (20.8, 62.5)	62.5 (39.6, 83.3)	62.5 (39.6, 83.3)
Missing, n	*18*	*928*	*1149*
Symptom burden	50.0 (25.0, 66.7)	66.7 (50.0, 83.3)	66.7 (50.0, 83.3)
Missing, n	*10*	*926*	*1149*
Total symptom score	44.8 (25.0, 64.6)	64.6 (43.8, 83.3)	62.5 (43.8, 83.3)
Missing, n	*10*	*926*	*1149*
Self-efficacy	75.0 (50.0, 87.5)	75.0 (50.0, 87.5)	75.0 (50.0, 87.5)
Missing, n	*22*	*937*	*1158*
Quality of life	41.7 (25.0, 58.3)	58.3 (33.3, 75.0)	58.3 (41.7, 75.0)
Missing, n	*17*	*933*	*1155*
Social limitation	33.3 (12.5, 58.3)	50.0 (31.2, 81.2)	50.0 (33.3, 81.2)
Missing, n	*246*	*1054*	*1231*
Overall summary score	41.1 (25.3, 57.8)	55.2 (38.5, 77.3)	55.2 (38.7, 76.4)
Missing, n	*0*	*923*	*1148*
Clinical summary score	43.2 (26.0, 61.4)	57.8 (38.9, 79.2)	57.3 (38.0, 78.1)
Missing, n	*1*	*923*	*1148*

Data are shown as median (Q1, Q3).

associations were similar in direction and magnitude to those identified in the main analyses, i.e. baseline health status and new-onset HF. Among patients with LVEF ≥40% or missing (online supplementary *Table S8.2*), health status was associated with age, race, country, chronic kidney disease, atrial fibrillation, and diabetes, as well as baseline health status and new-onset HF, but not with HF aetiology or smoking status.

Discussion

This analysis suggests nearly one-third of patients hospitalised with AHF were 'alive and well' 6 months later, and this generally persisted until at least 12 months. However, about 40% of patients who survived to 6 months had a persistently poor quality of life. These findings are important, given that many HF patients value quality of

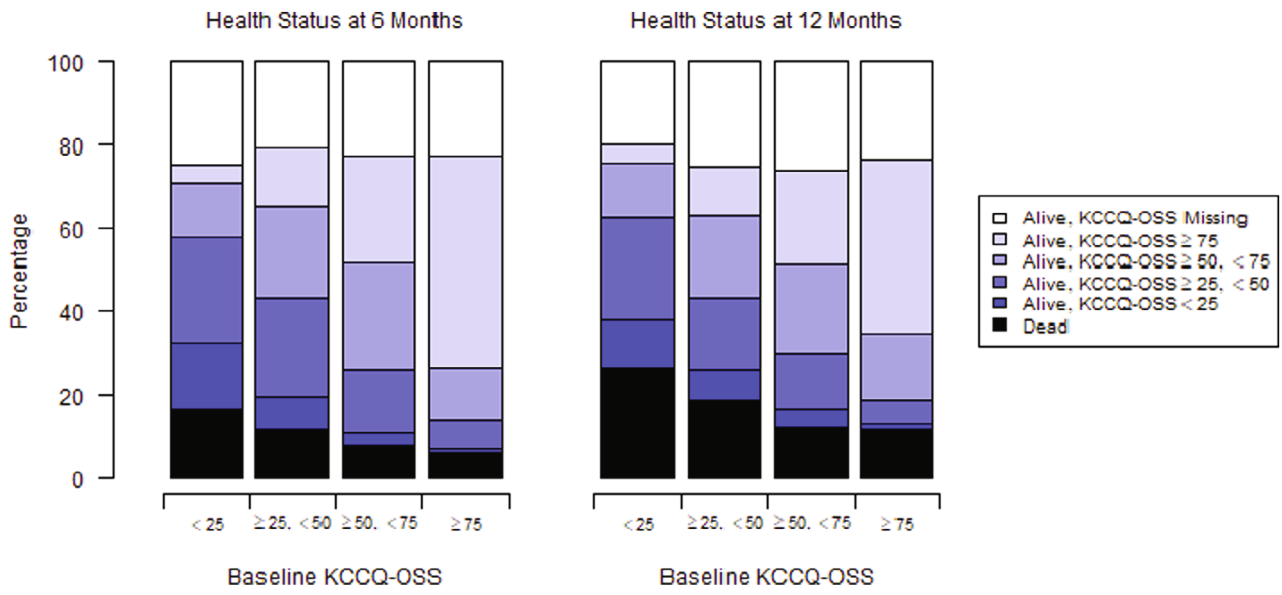


Figure 2 Health status at 6 and 12 months in relation to baseline Kansas City Cardiomyopathy Questionnaire overall summary score (KCCQ-OSS).

life as much or more than prognosis[1] and the growing interest in health status as a measure of quality of HF care.[2] A better understanding of patient characteristics associated with both poor and excellent post-discharge health status may identify patients who will benefit from further outpatient interventions aimed at controlling HF symptoms, managing comorbidities and improving health status. Our results also provide normative baseline data for future acute and chronic HFrEF and HF with preserved ejection fraction (HFpEF) studies designed to understand and improve the trajectory of KCCQ after AHF hospitalization.

After adjusting for known predictors of HF severity, new-onset HF had the strongest association with post-discharge health status, and this was consistent across our models. New-onset HF and HFrEF have historically been associated with high mortality, although findings have been mixed among observational studies. Patient age, underlying aetiology, and comorbid conditions likely play important roles.[9,12,19] Baseline KCCQ was also closely tied to excellent post-discharge health status. This suggests that patients who experienced rapid, complete response to in-hospital therapy predicts favourable outcomes after discharge, although it is also possible that these patients were less sick at the time of admission. Younger age and fewer comorbid conditions also appeared associated with a greater capacity to recover, particularly among those with HFpEF. The availability of multiple effective therapies may have contributed to better post-discharge health status for patients with HFrEF compared to those with HFpEF, for whom there were no effective therapies until recently and who were also older with more complex comorbidities.[20,21]

Exploration of associations with race and country was limited by differences in population demographics and healthcare systems across the enrolling countries, and it is notable that associations with race and country were not detected in post-hoc subgroup analysis of participants with HFrEF. In our study, 99% (685/695) of Black patients were enrolled in the USA, where health insurance is employment-based, and race is closely tied to social determinants of health. Health insurance was not included as a covariate in our multivariable models because the only included country without a universal healthcare system was the USA. Previous studies in the USA have found mixed results regarding the association of race with worse HF outcomes.[22–25] An analysis conducted in the Veterans Health Administration, which resembles universal healthcare, suggests differences in health outcomes between races may not be evident when healthcare access is equal.[26]

Women in this study were, on average, older and more often had HFpEF, making it difficult to disentangle age and underlying disease from potential associations with sex and health status. The odds of being 'alive and well' were 1.22 times better for men compared to women, although CIs did not reach the threshold for statistical significance.

Our data representing a broad international cohort provide new information regarding the natural history of health status more than 6 months after AHF hospitalization across multiple global regions and healthcare systems. Previous work generally focused on patients with stable HF, short-term trajectory of health status, or secondary analyses of clinical trials among carefully selected patients who may not represent the broader population of HF patients and HF care. Previous studies were secondary analyses of interventional or telemedicine trials and generally revealed modest but clinically important improvement in HF-specific quality of life, which was not always accompanied by reduction in AHF hospitalisation or mortality.[25,27–33]

Table 3 Multivariable logistic regression model for being 'alive and well' at 6 months, defined as alive with Kansas City Cardiomyopathy Questionnaire overall summary score (KCCQ-OSS) >75, and multivariable linear regression model for KCCQ-OSS at 6 months (using 12-month value if 6-month value not available)

Predictor	'Alive and well' (n = 2290[a])		Post-discharge KCCQ-OSS (n = 1984[b])	
	OR (95% CI)	p-value	β (95% CI)	p-value
Baseline KCCQ-OSS, per 10 points	1.47 (1.39, 1.55)	<0.0001	4.4 (4.0, 4.9)	<0.0001
Age, per 10 years	0.85 (0.77, 0.94)	0.0017	−0.9 (−1.8, 0.0)	0.0473
Sex, male vs. female	1.22 (0.94, 1.60)	0.1394	1.2 (−1.1, 3.4)	0.3154
Race		0.0065		0.1005
Black vs. Caucasian	0.41 (0.23, 0.74)		−6.6 (−11.9, −1.4)	
Asian vs. Caucasian	1.91 (0.66, 5.49)		0.8 (−9.5, 11.2)	
Other vs. Caucasian	0.58 (0.27, 1.25)		−1.5 (−8.6, 5.6)	
Country		<0.0001		0.3439
Russian Federation vs. USA	0.46 (0.30, 0.69)		−3.1 (−7.0, 0.7)	
Germany vs. USA	0.95 (0.62, 1.44)		−1.3 (−5.4, 2.8)	
Spain vs. USA	1.01 (0.63, 1.62)		−1.7 (−6.2, 2.8)	
Great Britain vs. USA	0.64 (0.39, 1.06)		−3.8 (−8.4, 0.9)	
New-onset HF vs. decompensated HF	2.63 (2.07, 3.35)	<0.0001	8.3 (6.1, 10.4)	<0.0001
LVEF		0.0021		0.0094
40%–50% vs. <40%	0.88 (0.63, 1.23)		−2.2 (−5.1, 0.8)	
>50% vs. <40%	0.60 (0.44, 0.82)		−2.8 (−5.5, −0.1)	
Not recorded vs. <40%	0.62 (0.44, 0.86)		−4.9 (−7.9, −2.0)	
HTN vs. no HTN	1.03 (0.78, 1.35)	0.8475	0.1 (−2.4, 2.6)	0.9619
AF vs. no AF	0.98 (0.77, 1.24)	0.8634	−2.3 (−4.3, −0.3)	0.0230
Diabetic vs. non-diabetic	0.83 (0.64, 1.06)	0.1293	−3.8 (−5.9, −1.8)	0.0003
CKD vs. no CKD	0.82 (0.62, 1.09)	0.1688	0.0 (−2.3, 2.2)	0.9746
CAD vs. no CAD	0.84 (0.64, 1.10)	0.2051	−2.6 (−4.9, −0.2)	0.0303
HF aetiology		0.3054		0.2107
Hypertensive vs. ischaemic	1.18 (0.79, 1.75)		1.4 (−1.7, 4.5)	
Cardiomyopathy vs. ischaemic	1.32 (0.90, 1.94)		3.3 (−0.2, 6.8)	
Valvular vs. ischaemic	1.49 (0.99, 2.25)		4.2 (0.5, 7.9)	
Other vs. ischaemic	1.22 (0.77, 1.94)		0.8 (−3.3, 4.9)	
Unknown vs. ischaemic	1.46 (1.03, 2.07)		2.4 (−0.6, 5.5)	
Smoking		0.9170		0.2854
Former vs. never	0.92 (0.66, 1.29)		1.5 (−1.5, 4.4)	
Current vs. never	1.03 (0.78, 1.35)		1.3 (−1.1, 3.8)	
Unknown vs. never	0.90 (0.45, 1.77)		−3.9 (−10.0, 2.3)	

AF, atrial fibrillation; CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; HF, heart failure; HTN, hypertension; LVEF, left ventricular ejection fraction; OR, odds ratio.
[a]Of 2295 subjects for whom 'alive and well' status could be determined, five subjects had missing data for one or more predictors.
[b]Of 1988 subjects for whom post-discharge KCCQ-OSS was available, four subjects had missing data for one or more predictors.

Clinical Implications

There is ongoing discussion regarding how best to use quality of life as an outcome measure in chronic and acute HF.[34] Recent initiatives have proposed health status as a measure of the quality of care for outpatients with HF.[5] The International Consortium for Health Outcomes Measurement has endorsed the KCCQ as part of its measurement set for outpatient quality assessment. In the USA, use of 30-day mortality and readmission as a surrogate measure of the quality of care for patients hospitalized with AHF (and for which poor performance leads to substantial financial penalties) has been under great scrutiny. Being 'alive and well' may be a more meaningful outcome for patients and therefore a better measure of the effectiveness of care. As the first report of such an outcome, we believe that this lays the foundation for considering new opportunities to measure the outcomes of patients with AHF and can lay the foundation for both clinical practice (developing population health strategies to identify and treat patients not meeting this measure) and for assessment of effectiveness of care.

Pronounced improvements in KCCQ following hospitalisation for AHF may be expected in a substantial proportion of patients who receive guideline-directed medical therapies. Thus, trials using KCCQ improvement post-hospitalisation as an outcome should be adequately powered to demonstrate incremental benefit of new therapies in this setting. Understanding the trajectory of health status recovery may assist in its adoption for AHF and help target treatments and systems of care to those most in need.[27,35]

Limitations

Our findings should be interpreted in the context of several potential limitations. First, because follow-up was not complete, we cannot rule out the possibility that patients with lower post-discharge health status were less likely to complete a KCCQ, although sensitivity analyses suggest that this was not the case. Second, it was not feasible to enrol a random sample of patients hospitalized with AHF, thus our findings may not be generalizable to all AHF patients. Third, only patients who provided written informed consent were enrolled, except in rare cases where a guardian was available and willing to do so on their behalf. This effectively excluded patients who were critically ill and accounts for the low mortality during the index hospitalisation. Fourth, we were not able to examine potential effect modification by unmeasured factors such as medication non-adherence, or recurrent hospitalisation. Participants were enrolled between 2014 and 2016, before ivabradine and angiotensin receptor–neprilysin inhibitor (ARNi) were widely available. For patients lacking health insurance, these medications may have been unaffordable. This may account for the low use of these agents. While the use of ivabradine and ARNi may improve quality of life in chronic HFrEF,[27,36] analyses of randomised trials and current registries of patients taking these and other modern HF medications are ongoing to understand their potential impact on health status after hospitalisation for AHF. Fifth, criteria for AHF diagnosis reflected local practice, and only the results of routine investigations were recorded in REPORT-HF, which may not have included tests of renal function in all countries.[8] Also, in common with most registries and trials, the results of tests that were done were not always recorded. Finally, fewer than 25% of our patients were aged >80 years and so our findings may not generalize as well to such patients.

Conclusions

In this international global registry across several world regions, health status recovery after AHF hospitalisation was highly variable. Those with the best health status at 6 months were younger, had new-onset HFrEF and a higher baseline KCCQ. Nearly one-third of survivors were 'alive and well' several months post-discharge. Investigating reasons for both failure and success might identify new therapeutic targets to improve outcomes. Efforts to improve survival for AHF should not neglect the importance of surviving 'well'.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Conflict of interest: J.G.C. reports receiving personal fees from Johnson & Johnson during the conduct of the study; grants and personal fees from Amgen, Bayer, Bristol Myers Squibb, Philips, Stealth Biopharmaceuticals, and Torrent Pharmaceuticals; personal fees from AstraZeneca, GSK, Myokardia, Sanofi, and Servier; grants, personal fees, and non-financial support from Medtronic, Novartis, and Vifor; and grants and non-financial support from Pharmacosmos and PharmaNord. J.A.S. discloses consulting fees from Novartis and intellectual property ownership of the KCCQ. Unrelated to this project, he discloses serving as a consultant on patient-reported outcome to Bayer, Amgen, Myokardia, Merck and Jannsen; owning the copyright to the SAQ and KCCQ, serving on a Scientific Advisory Board for United Healthcare and on the Board of Directors of Blue Cross Blue Shield of Kansas City. He has an equity ownership in Health Outcomes Sciences. C.E.A. reports receiving grants and personal fees from Novartis related to REPORT-HF; serving on steering committees in trials and/or registries sponsored by Abbott, Boehringer Ingelheim, Novartis, and Vifor outside of REPORT-HF; receiving grants and personal fees from Abbott, Boehringer Ingelheim, Novartis, and Vifor; non-financial support from the University Hospital Würzburg and the Comprehensive Heart Failure Center Würzburg; and grant support from the German Ministry for Education and Research. G.F. reports receiving research grants from the European Union, committee fees from Novartis related to REPORT-HF, and serving as a committee member in trials and/or registries sponsored by Servier, Boehringer Ingelheim, Medtronic, and Vifor. U.D. reports serving in steering committees in trials/registries sponsored by Novartis and Amgen outside the REPORT-HF and receiving grants and personal fees from AstraZeneca, Pfizer, Novartis, Amgen, Vifor Pharma, Boehringer Ingelheim, Boston Scientific and Roche Diagnostics outside the REPORT-HF. A.S. is employed by Novartis Pharma AG and owns Novartis shares. G.E. reports counseling of Abbott, Astra, Boehringer Ingelheim, Novartis and Vifor. M.G. is a former employee of Novartis Pharma AG. S.P.C. reports receiving research support from the National Institutes of Health, Association for Healthcare Research and Quality, American Heart Association, and Patient-Centered Outcomes Research Institute, and serving as a paid consultant for Novartis, Ortho Clinical, Boehringer Ingelheim and Vixiar. J.T. is supported by the National University of Singapore Start-up grant, the tier 1 grant from the ministry of education and the CS-IRG New Investigator Grant from the National Medical Research Council; has received consulting or speaker fees from Daiichi-Sankyo, Boehringer Ingelheim, Roche diagnostics and Us2.ai, owns patent US-10702247-B2 unrelated to the present work.

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