Health Status Identifies Heart Failure Outpatients at Risk for Hospitalization or Death

Paul A. Heidenreich, MD, MS,* John A. Spertus, MD, MPH,† Philip G. Jones, MS,†
William S. Weintraub, MD,‡ John S. Rumsfeld, MD, PhD,§ Saif S. Rathore, MPH,‖
Eric D. Peterson, MD, MPH,¶ Frederick A. Masoudi, MD, MSPH,# Harlan M. Krumholz, MD, MS,‖
Edward P. Havranek, MD,# Mark W. Conard, PhD,† Randall E. Williams, MD,**
for the Cardiovascular Outcomes Research Consortium

Palo Alto, California; Kansas City, Missouri; Atlanta, Georgia; Denver, Colorado; New Haven, Connecticut; Durham, North Carolina; Evanston, Illinois

OBJECTIVES	We tested the hypothesis that one health status measure, the Kansas City Cardiomyopathy Questionnaire (KCCQ), provides prognostic information independent of other clinical data in outpatients with heart failure (HF).
BACKGROUND	Health status measures are used to describe a patient's clinical condition and have been shown to predict mortality in some populations. Their prognostic value may be particularly useful among patients with HF for identifying candidates for disease management in whom increased care may reduce hospitalizations and prevent death.
METHODS	We evaluated 505 HF patients from 13 outpatient clinics who had an ejection fraction <40% using the KCCQ summary score. Proportional hazards regression was used to evaluate the association between the KCCQ summary score (range, 0 to 100; higher scores indicate better health status) and the primary outcome of death or HF admission, adjusting for baseline patient characteristics, 6-min walk distance, and B-type natriuretic peptide (BNP).
RESULTS	The mean age was 61 years, 76% of patients were male, 51% had an ischemic HF etiology, and 5% were New York Heart Association functional class IV. At 12 months, among the 9% of patients with a KCCQ score <25, 37% had been admitted for HF and 20% had died, compared with 7% (HF admissions) and 5% (death) of those with a KCCQ score ≥75 (33% of patients, p < 0.0001 for both comparisons). In sequential multivariable models adjusting for clinical variables, 6-min walk, and BNP levels, the KCCQ score remained significantly associated with survival free of HF hospitalization.
CONCLUSIONS	A low KCCQ score is an independent predictor of poor prognosis in outpatients with HF. (J Am Coll Cardiol 2006;47:752–6) © 2006 by the American College of Cardiology Foundation

Providers routinely rely on crude surrogates for health status, particularly the New York Heart Association (NYHA) class, in their management of patients with heart failure (HF). The assessment, however, is generally subjective and poorly standardized, and is based on the clinician's opinion of the relative importance of different symptoms on patients' function. Recently, efforts have been made to standardize the evaluation of health status from the patient's perspective, both for use as an outcome in clinical trials and as an aid for clinical management. One such instrument, The Kansas City Cardiomyopathy Questionnaire (KCCQ), is a HF-specific measure of health status and quality of life (1). It has been proven to be reliable and highly responsive to clinical changes deemed important by cardiologists (1).

Health status measures may be important in the clinical care of patients with cardiovascular disease not only because they are responsive to an increasing emphasis on patient-centered outcome measures, but also because they may be independently predictive of morbidity and mortality. In this study, we sought to determine whether the KCCQ is associated with survival and future hospitalization for outpatients with HF.

METHODS

Study population. Patients were recruited through the Cardiovascular Outcomes Research Consortium. A list of participating investigators and institutions is provided in the Appendix. A total of 547 outpatients were enrolled at 13 North American centers, with a range of 3 to 82 (median, 43) patients per site. Eligibility criteria included patients' awareness of their HF diagnosis, an ejection fraction <40%, age >30 years, a willingness to provide informed consent, and either a HF diagnosis in their outpatient medical record or a hospitalization for decompensated HF within the previous three years. Institutional review board approval at each site was secured before study implementation.

Health status questionnaire. The KCCQ is a 23-item, self-administered questionnaire that quantifies physical function, symptoms, social function, self-efficacy, and quality of life for patients with HF. The validity and reliability and responsiveness to clinical change of this questionnaire have been previously established (1). The KCCQ summary score integrates information from the physical limitation, symptom, social limitation, and quality of life scales and was used for all analyses. The range for this scale is 0 to 100; higher scores reflect better health status (symptoms, function, and quality of life).

Study protocol. A complete history and physical examination were conducted, and included a NYHA functional classification and a 6-min walk test (the distance in meters walked by a patient indoors on level ground in 6 min) (2). Throughout the initial phase of the study, point-of-care instruments capable of measuring B-type natriuretic peptide (BNP) levels (3) were distributed to the sites (Biosite Inc., San Diego, California). An administrative delay in their distribution resulted in BNP assessments being available for 328 (65%) of patients with follow-up data. No significant differences in age, gender, race, HF etiology, or physician's classification of change in HF status were present between those with and without BNP assessments.

Table 1. Patient Characteristics

	Kansas City Cardiomyopathy Questionnaire Summary Score				
	<25	25–49	50–74	≥75	p Value
n	43	125	172	165	
Age (yrs)	59 ± 15	60 ± 14	61 ± 13	63 ± 12	0.40
Male	30 (70%)	93 (74%)	129 (75%)	130 (79%)	0.61
Caucasian	27 (63%)	84 (67%)	118 (69%)	112 (69%)	0.88
NYHA functional class					
I	0 (0%)	3 (2%)	13 (8%)	40 (24%)	<0.001
II	3 (7%)	36 (29%)	81 (47%)	90 (55%)	—
III	28 (65%)	79 (63%)	70 (41%)	34 (21%)	—
IV	12 (28%)	7 (6%)	8 (5%)	0 (0%)	—
Ejection fraction (%)	23 ± 7	24 ± 8	25 ± 8	26 ± 8	0.06
Ischemic cause of heart failure	16 (40%)	61 (49%)	86 (53%)	88 (54%)	0.41
Hypertension	26 (61%)	71 (57%)	90 (52%)	99 (60%)	0.51
Diabetes	18 (42%)	45 (36%)	58 (34%)	48 (29%)	0.37
Pulmonary disease	9 (21%)	29 (23%)	32 (19%)	26 (16%)	0.44
Atrial fibrillation or flutter	10 (23%)	37 (30%)	58 (34%)	50 (30%)	0.59
Prior myocardial infarction	12 (28%)	50 (40%)	76 (44%)	62 (38%)	0.24
Renal failure	4 (9%)	7 (6%)	11 (6%)	7 (4%)	0.61
Prior stroke	4 (9%)	13 (10%)	13 (8%)	14 (9%)	0.86
Medication use					
ACE inhibitor	37 (86%)	99 (79%)	141 (82%)	139 (84%)	0.64
Angiotensin receptor blocker	4 (9%)	23 (18%)	25 (15%)	23 (14%)	0.49
Beta-blocker	30 (70%)	97 (78%)	128 (74%)	128 (78%)	0.67
Digoxin	30 (70%)	88 (70%)	102 (59%)	90 (55%)	0.03
Spironolactone	15 (35%)	55 (44%)	63 (37%)	53 (32%)	0.22
Diuretic	40 (93%)	108 (86%)	142 (83%)	125 (76%)	0.02
Calcium antagonist	5 (12%)	13 (10%)	11 (6%)	20 (12%)	0.32
Physical examination					
Systolic blood pressure (mm Hg)	111 ± 28	116 ± 21	121 ± 25	128 ± 20	<0.001
Diastolic blood pressure (mm Hg)	69 ± 18	68 ± 15	68 ± 14	71 ± 13	0.26
Pulse	78 ± 17	77 ± 14	72 ± 14	71 ± 14	<0.001
Jugular venous distension ≥10 cm	16 (41%)	18 (17%)	26 (17%)	9 (6%)	<0.001
S3	13 (30%)	18 (14%)	29 (17%)	19 (12%)	0.024
Rales	8 (19%)	17 (14%)	19 (11%)	11 (7%)	0.09
Body mass index	30 ± 9	30 ± 9	29 ± 7	29 ± 7	0.59
Test results					
6-min walk test (ft)	590 ± 325	806 ± 328	992 ± 355	1161 ± 363	<0.001
B-type natriuretic peptide (ng/dl)	315 ± 367	429 ± 421	433 ± 400	310 ± 343	0.05

Data were missing for B-type natriuretic peptide (177), jugular veins (61), 6-min walk (32), failure etiology (15), blood pressure (3), body mass index (3), NYHA functional class (3), race (3), age (2), and pulse (1).
ACE = angiotensin-converting enzyme; NYHA = New York Heart Association.

Outcome. The primary outcome was survival free of HF hospitalization at one year. Secondary outcomes included hospitalization for HF and total mortality.

Statistical approach. Baseline characteristics of the study population are presented as frequencies and percentages for categorical variables and as mean ± SD for continuous variables. Differences between patients grouped by KCCQ score were evaluated using analysis of variance for continuous variables and chi-square tests for categorical variables. Differences in survival were evaluated with the log-rank test. Proportional hazards analysis was used to compare survival for patients grouped by KCCQ score while adjusting for baseline characteristics (age, gender, race, diabetes, hypertension, ejection fraction, ischemic cause of HF, obstructive pulmonary disease or asthma, atrial fibrillation or flutter, prior myocardial infarction, renal failure, prior stroke, systolic blood pressure, diastolic blood pressure, pulse, jugular venous distension, S3, and rales). In multivariable analysis, BNP levels were grouped into quartiles and the KCCQ was separated by ranges of 25 points. This latter framework was adopted to simplify interpretation of KCCQ scores in future applications. Statistical analyses were performed using SAS version 8.02 (SAS Institute, Cary, North Carolina).

RESULTS

Patient characteristics. A total of 547 outpatients were enrolled. The mean age of the population was 61 years, 76% of patients were male, 51% had an ischemic HF etiology, and 5% were NYHA functional class IV. Of these, one-year follow-up was available in 505 (92%). Those without follow-up were not significantly different from those with follow-up for any of the demographic and clinical variables listed in Table 1.

The summary KCCQ score was below 25 (lowest health status) in 43 (9%) patients, 25 to 49 in 125 (25%) patients, 50 to 74 in 172 (34%) patients, and 75 or more in 165 (33%)
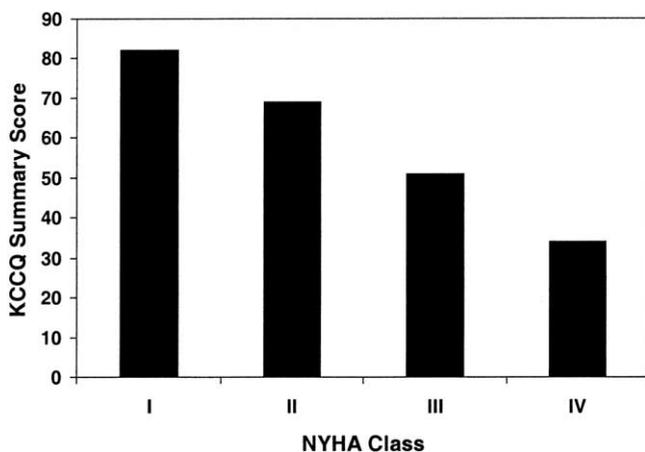
Figure 1. The association between the Kansas City Cardiomyopathy Questionnaire (KCCQ) summary score and New York Heart Association (NYHA) functional class is shown. Patients with lower scores had a higher NYHA functional class.
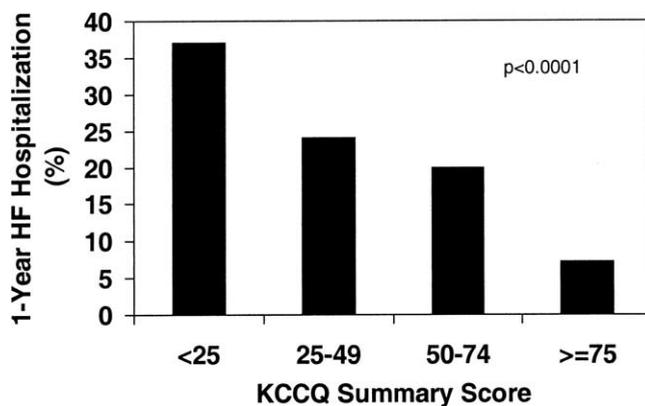
Figure 2. One-year hospitalization for heart failure (HF) is shown for patients grouped by Kansas City Cardiomyopathy Questionnaire (KCCQ) summary score. Those with the lowest scores had the highest rate of heart failure admission.

patients. Baseline demographic, clinical, and health status characteristics by KCCQ score group are listed in Table 1. Patients with lower KCCQ scores were more likely to have a higher NYHA functional class (Fig. 1). Lower KCCQ scores were also associated (p < 0.05) with a lower systolic blood pressure, a higher pulse rate, greater jugular venous distension, a shorter 6-min walk distance, and treatment with diuretics and digoxin. Trends (p < 0.10) were observed for a higher prevalence of rales, a lower ejection fraction, and a higher BNP level in those with lower KCCQ scores.

HF hospitalizations and survival. There were 124 (24.6%) patients that either died (n = 56) or were hospitalized for HF during the one-year follow-up period. Patients with lower KCCQ scores had more hospitalizations for HF than those with higher scores (Fig. 2). When compared with those with a KCCQ score of 75 or greater, those with a score <25 were five times as likely to be hospitalized for HF during the next year (37% vs. 7%).

Mortality increased with decreasing KCCQ score (Fig. 3). One-year mortality was four-fold greater in those with a KCCQ score <25 compared with those with a score of 75 or greater (20% vs. 5%). The relationship between KCCQ score group and the primary outcome, survival free of hospitalization for HF, is shown in Figure 4. Differences in survival free from HF hospitalization between high and low KCCQ score groups were noted by one month and continued to widen over time. At one year, 45% of patients with KCCQ scores <25 had died or been hospitalized for HF compared with 12% for those with KCCQ scores of 75 or greater.

In multivariable proportional hazards analysis, the KCCQ score remained predictive of survival free from HF hospitalization after adjustment for clinical characteristics (Table 2). Although adjustment for BNP levels reduced the sample size by 44%, both BNP (p = 0.005) and KCCQ score (p = 0.007) were independently associated with survival free from HF hospitalization.
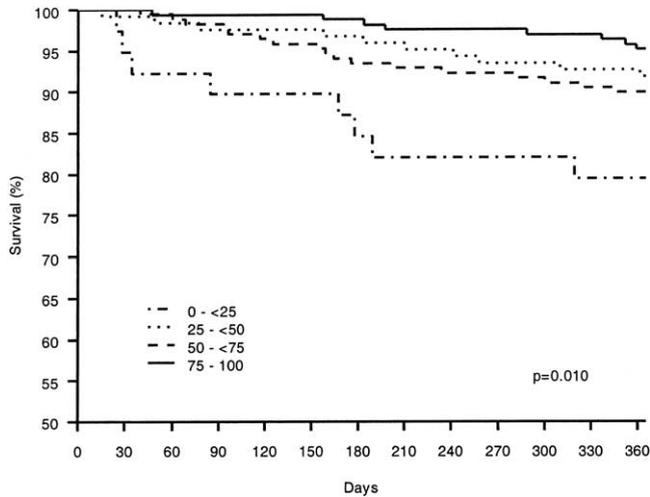
Figure 3. All-cause mortality is shown for outpatients with heart failure grouped by Kansas City Cardiomyopathy Questionnaire (KCCQ) summary score. Those with the lowest scores had the highest mortality.

DISCUSSION

Heart failure is characterized by both poor survival and frequent hospitalizations, but the course of individual patients is highly variable (4). Several clinical characteristics have been identified that are associated with a poor prognosis, including physical examination (S3, elevated jugular venous pressure) (5), low ejection fraction (6), and laboratory findings (e.g., anemia) (7). Health status as estimated by the physician using the NYHA functional classification has also been associated with outcome (4,8). In this study we have shown that poor health status defined by the patient's KCCQ responses is also associated with worse prognosis. In those with a score <25, the rate of HF hospitalization was five-fold greater and total mortality was four-fold greater at one year compared with those with scores of at least 75. These results extend a recently reported
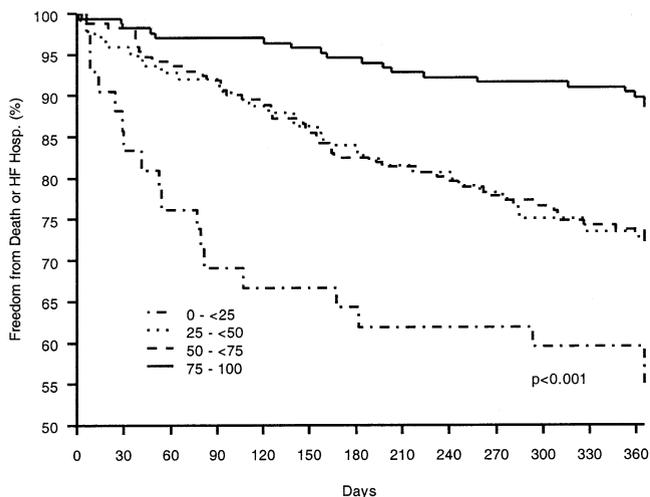

Figure 4. Survival free from heart failure hospitalization is shown for outpatients according the baseline Kansas City Cardiomyopathy Questionnaire (KCCQ) summary score. Patients with the lowest scores had the worse event-free survival.

Table 2. KCCQ Score and Event-Free Survival: Multivariable Adjustment

	Hazard Ratio	95% Confidence Interval	p Value
Model 1 (no adjustment)			
KCCQ score (vs. ≥75)			<0.0001
50–74	2.69	1.25–3.71	
25–49	2.72	1.13–3.76	
<25	5.33	1.32–5.82	
Model 2 (adjustment for clinical variables*)			
KCCQ score (vs. ≥75)			0.003
50–74	2.18	1.23–3.86	
25–49	2.32	1.28–4.25	
<25	3.82	1.87–7.79	
Model 3 (clinical variables and 6-min walk)			
KCCQ score (vs. ≥75)			0.02
50–74	2.15	1.25–3.71	
25–49	2.06	1.13–3.76	
<25	2.77	1.32–5.82	

*The following clinical variables were tested and included in the model (boldface type) if they were significantly associated (p < 0.05) with event-free survival: age, gender, race, **diabetes,** hypertension, ejection fraction, ischemic cause of heart failure, obstructive pulmonary disease or asthma, **atrial fibrillation or flutter,** prior myocardial infarction, renal failure, prior stroke, systolic blood pressure, diastolic blood pressure, pulse, **jugular venous distension, S3,** and rales.
KCCQ = Kansas City Cardiomyopathy Questionnaire.

analysis of the EPlerenone's neuroHormonal Efficacy and SUrvival Study (EPHESUS) trial that described an association of KCCQ scores with survival and hospitalization by including patients with a broader range of HF etiologies, avoiding the potential selection biases of a clinical trial, and by assessing stable outpatients rather than those recently admitted with a myocardial infarction (9). All of these considerations increase the generalizability of these findings and the potential applicability of the KCCQ in clinical care.

A patient-derived measure that predicts outcome is potentially useful for several reasons. First, our study found that the summary score from the KCCQ provides additional information to standard demographic, clinical, and laboratory data. Specifically, the KCCQ summary score provided prognostic information independent of these standard characteristics, even when supplemented with six-min walk distance and BNP level. Thus, including the KCCQ summary score can improve prognosis estimates for individual patients. An important advantage of the KCCQ in stratifying risk is that it does not require a physical examination, phlebotomy, or other specialized or invasive training. Thus, surveying populations of patients to identify those at greatest risk may be an important method for identifying high-risk patients from among a large population of HF outpatients.

Accordingly, an important potential application of this information is to identify candidates for more intensive therapy, including cardiology referral and HF programs. Several trials have found that patients with symptomatic HF have reduced hospitalizations and in some cases reduced mortality when enrolled in programs that use a combination

of education, home monitoring, and medication management (10,11). High-risk patients are the best candidates for these programs; however, estimating risk is expensive if it requires a physician visit or additional laboratory tests. Currently, administrative data, which suffer from limited diagnostic accuracy, are all that is available to most health care organizations. Alternatively, organizations can mail the KCCQ to patients identified from administrative data as having HF and identify those with the lowest scores (worse status) to enroll in HF programs or to target for additional interventions (e.g., referral to cardiologists).

The KCCQ provides several potential advantages over the NYHA functional status classification. As previously noted, the KCCQ is derived from patients, whereas the NYHA class is determined by the clinician. Therefore, the NYHA functional class is by definition subjective and may unintentionally be influenced by ejection fraction or other data available to the physician. The standardized assessment makes the KCCQ a "more pure" measure of a patient's symptoms and functional status. Finally, the KCCQ includes the full range of patient health status (symptoms, functional status, and health-related quality of life). Health-related quality of life is not included in NYHA functional classification, and yet multiple studies have shown that health-related quality of life is predictive of subsequent mortality in different cardiac populations (12–14).

Also in keeping with the results of this investigation, studies using the Minnesota Living with Heart Failure Questionnaire have found that survival is greater for patients with better health status, independent of ejection fraction and NYHA functional class (13,14). Additional studies are needed to determine the relative prognostic value of the KCCQ and the Minnesota Questionnaire.

Our study has several potential limitations. Most patients were enrolled at outpatient clinics of academic medical centers, and their mean age is less than that of patients in the community (4). However, we have no reason to believe that the association between health status and outcome is different at academic and non-academic centers. We included only patients with systolic dysfunction; thus, it is unclear whether the KCCQ predicts outcome for patients with HF because of isolated diastolic dysfunction or valvular disease. Finally, additional studies are needed to document that using the summary score of the KCCQ results in better triage and care for HF patients.

In conclusion, this study found that a low KCCQ summary score is associated with increased mortality and hospitalization for HF. This increase in risk with a low KCCQ score was independent of clinical characteristics, including the 6-min walk distance and the BNP level. The KCCQ is an attractive and inexpensive method of estimating a HF patient's prognosis for the individual physician or the health plan interested in identifying high-risk patients for specific interventions.

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APPENDIX

For a list of the members of the Cardiovascular Outcomes Research Consortium, please see the online version of this article.