Identifying Heart Failure Patients at High Risk for Near-Term Cardiovascular Events With Serial Health Status Assessments

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Background—Identification of heart failure outpatients at increased risk for clinical deterioration remains a critical challenge, with few tools currently available to assist clinicians. We tested whether serial health status assessments with the Kansas City Cardiomyopathy Questionnaire (KCCQ) can identify patients at increased risk for mortality and hospitalization.

Methods and Results—We evaluated 1358 patients with heart failure after an acute myocardial infarction in the Eplerenone's Neurohormonal Efficacy and Survival Study, a multicenter randomized trial that included serial KCCQ assessments. Cox proportional-hazards models were used to examine whether changes in KCCQ scores during successive outpatient visits were independently associated with all-cause mortality and cardiovascular mortality or hospitalization. Change in KCCQ (ΔKCCQ) was linearly associated with all-cause mortality (hazard ratio [HR], for each 5-point decrease in ΔKCCQ, 1.11; 95% CI, 1.04 to 1.19) and the combined outcome of cardiovascular mortality or hospitalization (HR for each 5-point decrease in ΔKCCQ, 1.12; 95% CI 1.07 to 1.18). In Kaplan-Meier survival analysis, all-cause mortality among patients with ΔKCCQ of ≤ -10, > -10 to < 10, and > 10 points was 26%, 16%, and 13%, respectively ($P=0.008$). After multivariable adjustment, the linear relationship between ΔKCCQ and both all-cause mortality and combined cardiovascular death and hospitalization persisted (HR, 1.09; 95% CI, 1.00 to 1.18; and HR, 1.11; 95% CI, 1.05 to 1.17 for each 5-point decrease in ΔKCCQ, respectively).

Conclusions—In heart failure outpatients, serial health status assessments with the KCCQ can identify high-risk patients and may prove useful in directing the frequency of follow-up and the intensity of treatment. **(*Circulation*. 2007;115: 1975-1981.)**

Key Words: health status ■ heart failure ■ mortality ■ prognosis ■ risk factors

Heart failure (HF) is a highly prevalent, costly, and chronic condition associated with high symptom burden, mortality, and hospital admission rates.[1] Typically, the physician–patient relationship is longitudinal, which permits serial monitoring of a patient's condition and treatment over time. A critical challenge in caring for outpatients with HF is to identify patient factors that can predict clinical deterioration. Although many cross-sectional predictors of adverse outcomes have been determined in outpatients with HF,[2–21] few clinical tools are available at the point of care to help physicians interpret changes in patients' clinical condition over time. Yet, serial monitoring of HF patients' clinical status is a fundamental tenet of current clinical guidelines.[22] What is needed is a system capable of predicting clinical outcomes that is patient centered, sensitive to clinical change, scalable, and easy to administer. Such a system could be an important aid to clinicians in determining the frequency of outpatient follow-up and directing changes in therapy that could potentially improve patient outcomes.

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One potential candidate for such a system is serial assessments of health status, which formally quantify patients' symptoms, function, and quality of life. The Kansas City Cardiomyopathy Questionnaire (KCCQ)[23] is an example of a validated disease-specific measure for HF that is patient oriented, easy to administer, and highly sensitive to change in patients' clinical status.[24] A single baseline health status assessment with KCCQ has previously been shown to be prognostically important.[25] However, it is unknown whether

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dynamic changes in health status over time, as measured by serial KCCQ assessments, can identify patients at high risk for mortality and hospital readmission.

To address this question, we studied the relationship between changes in KCCQ scores among HF outpatients and subsequent cardiovascular mortality and hospitalization over 14 months of follow-up. We analyzed data from the Eplerenone's Neurohormonal Efficacy and Survival Study (EPHESUS), a randomized, controlled trial of aldosterone blockade in patients with HF after acute myocardial infarction (MI). The EPHESUS study provided an ideal opportunity to address this issue, given the availability of detailed clinical information, close follow-up, and serial measurements of health status over time.

Methods

Patient Population

EPHESUS was a multicenter, randomized clinical trial evaluating the effect of eplerenone, a selective aldosterone blocker, on morbidity and mortality of patients with HF after acute MI between December 27, 1999, and December 31, 2001. Details of inclusion and exclusion criteria and study design have been given previously.[26,27] Briefly, 6632 patients with documented acute MI, left ventricular ejection fraction ≤40%, and postinfarction HF or diabetes were randomized to eplerenone or placebo and followed up serially at 1, 3, 6, and 12 months. Important exclusion criteria included serum creatinine concentration >2.5 mg/dL and potassium levels >5.0 mmol/L.

For the purposes of this analysis, we considered only patients who participated in the EPHESUS quality-of-life substudy (n=2280). All participating patients from Argentina, Brazil, Canada, France, Germany, the Netherlands, Spain, the United Kingdom, and the United States were enrolled in the quality-of-life substudy. In addition to standard clinical follow-up, these patients had serial evaluations of their health status with the KCCQ, a self-administered 23-item instrument with established reliability, validity, clinical responsiveness, and prognostic importance.[23–25,28]

Given acute changes in patients' health status during hospitalization, we chose 1 month after randomization as the baseline for this analysis. Median time from randomization to the 1-month follow-up visit was 27 days (interquartile range, 23 to 30 days). Because we wanted to focus on patients with post-MI HF, we subsequently excluded patients with diabetes mellitus but no HF symptoms at the time of randomization. The prognostic importance of the 1-month KCCQ in this patient population was previously documented.[25] The purpose of the present study was to evaluate the additional incremental prognostic value of serial KCCQ measurements during outpatient follow-up. Thus, our cohort included only patients who survived to their 3-month follow-up visit and completed health status assessments at both 1 and 3 months (n=1358).

Health Status Assessments

Assessments of patients' health status at 1 and 3 months were performed with linguistically and culturally validated versions of the KCCQ. The KCCQ is a self-administered, disease-specific, 23-item health status instrument for patients with HF that, on average, requires 4 to 6 minutes to complete.[23] The value of disease-specific health status measures compared with generic tools has been demonstrated previously.[29] The KCCQ quantifies several health status domains that include physical limitations, symptoms (frequency, severity, and recent change over time), self-efficacy, social function, and quality of life. Each scale is transformed to a score of 0 to 100; higher scores indicate better health status. To summarize the multiple domains of health status quantified by the KCCQ, an overall summary score (KCCQ-os) has been developed that includes the physical limitation, symptoms, quality of life, and social function domains of the KCCQ. Previous work has established that a 5-point change in the KCCQ-os represents a clinically important difference.[30]

Independent Variables

Independent variables were KCCQ-os at 1 month after enrollment in EPHESUS (the baseline assessment for the present study) and the change in KCCQ-os (ΔKCCQ-os) between the 1- and 3-month assessments (calculated by subtracting the KCCQ-os score at 1 month from the 3-month KCCQ-os scores).

In a subsidiary analysis, we used the data from the 3- and 6-month visits (instead of the 1- and 3-month visits). In this analysis, the 3-month KCCQ-os was considered baseline, and ΔKCCQ-os was calculated by subtracting the 3-month KCCQ-os score from the 6-month KCCQ-os score.

Outcome Assessment

The outcomes were all-cause mortality and the combined end point of cardiovascular mortality or hospital readmission for a cardiovascular event, a term that includes recurrent MI, HF, stroke, or ventricular arrhythmia. Patients were followed up for a mean of 14 months, starting with their 3-month outpatient visit. All end points were adjudicated by a blinded critical-events committee. Definitions of all adjudicated end points have been published elsewhere.[26,27]

Statistical Analysis

We first tested the unadjusted association of 1-month KCCQ-os with each outcome so that the additional incremental prognostic value of ΔKCCQ-os could be demonstrated. The unadjusted association between 1-month KCCQ-os and each outcome was tested through Cox regression analysis, with 1-month KCCQ-os analyzed as a continuous variable. In addition, unadjusted Kaplan-Meier survival analysis was performed with 1-month KCCQ-os analyzed as a categorical variable (On the basis of prior studies, patients were stratified into the following groups: 1-month KCCQ-os <25, 25 to <50, 50 to <75, and 75 to 100).

The crude (adjusted for 1-month KCCQ-os only) association between ΔKCCQ-os and each outcome was tested with Cox regression analysis, with ΔKCCQ-os entered as a continuous variable. To demonstrate that the prognostic value of ΔKCCQ-os is independent of traditional physician-based assessments of patients' functional status, Cox regression models were subsequently adjusted for both baseline New York Heart Association (NYHA) class and change in NYHA class between 1 and 3 months of follow up. Crude Kaplan-Meier survival analysis also was performed, with ΔKCCQ-os modeled as a categorical variable to facilitate clinical interpretability of change in KCCQ-os scores (ΔKCCQ-os ≤−10, >−10 to <10, and >10).

Multivariable Cox regression models were then constructed to assess whether the prognostic impact of baseline KCCQ-os and 2-month change in KCCQ-os (the difference between patients' 1- and 3-month scores) were independent of other patient characteristics. Model covariates included demographic characteristics (age, gender, race), medical history and comorbidities (prior HF, prior MI, prior angina, hypertension, dyslipidemia, diabetes mellitus, prior atrial fibrillation, stroke, chronic lung disease), disease severity at the time of randomization (pulmonary edema, Killip class, left ventricular ejection fraction after MI, use of reperfusion therapy), body mass index at study baseline (1-month visit), and vital signs (heart rate, systolic and diastolic blood pressures), laboratory values (sodium, glomerular filtration rate), and medications at the 1-month visit (angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, β-blockers, diuretics, and 3-Hydroxy-3-Methyl-Glutaryl-CoA reductase inhibitors [statins]). All Cox regression models included stratification by enrollment site and adjustment for patients' randomized treatment group. In addition, models assessing the independent prognostic impact of ΔKCCQ-os were adjusted for baseline 1-month KCCQ-os values. One-month KCCQ-os and ΔKCCQ-os were entered into the models as both continuous and categorical variables, as described above. Nonlinear trends for all continuous variables were tested through the use of restricted cubic

splines. Finally, we also tested for an interaction between 1-month KCCQ-os and ΔKCCQ-os to assess whether the prognostic value of ΔKCCQ-os varied depending on baseline health status.

To demonstrate the reproducibility of our findings, we also conducted several subsidiary analyses. In the first analysis, multivariable models were replicated using data from the 3- and 6-month visits (instead of the 1- and 3-month visits). In a second subsidiary analysis, additional models were constructed, adjusting the association between 1- to-3 month ΔKCCQ-os and outcomes for the 1- to 3-month change in systolic blood pressure, heart rate, and body mass index. All analyses were conducted with SAS 9.1 (SAS Institute, Inc, Cary, NC) and R version 2.3.1.[31] The institutional review board or ethics committee at each site involved in the EPHESUS trial approved the protocol, and all patients provided written informed consent before enrollment.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Baseline Characteristics

The baseline (1-month) characteristics of the study population are summarized in the Table. The mean age was 63 years, and 74% of patients were men. Reperfusion therapy at the time of their index MI was performed on 61% of patients. The mean post-MI left ventricular ejection fraction was 32%. The mean KCCQ-os on entry into the study was 70. Eighty-nine percent of patients were on angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, 75% were receiving β-blocker therapy, and 64% were on statin therapy. At 1 month, 43 patients (3%) had KCCQ-os <25, whereas 216 (16%) had KCCQ-os of 25 to <50, 460 (34%) had KCCQ-os of 50 to <75, and 639 (37%) had KCCQ-os of 75 to 100. For the 1- to 3-month ΔKCCQ-os, 193 patients (14%) had ≤−10 points ΔKCCQ-os, whereas 720 (53%) had ΔKCCQ-os >−10 to <10, and 445 (33%) had ΔKCCQ-os >10 points.

Predictive Value of Baseline (1-Month) KCCQ Overall Score

In unadjusted analyses, lower 1-month KCCQ-os scores were linearly associated with higher all-cause mortality (hazard ratio [HR] for each 5-point decrease in 1-month KCCQ-os, 1.05; 95% CI, 1.00 to 1.11) and higher combined cardiovascular mortality or hospitalization (HR for each 5-point decrease in 1-month KCCQ-os, 1.09; 95% CI, 1.06 to 1.13). In Kaplan-Meier survival analysis, 2-year all-cause mortality among patients with 1-month KCCQ-os scores of <25, 25 to <50, 50 to <75, and 75 to 100 was 28%, 17%, 20%, and 12.5%, respectively ($P=0.01$). Combined 2-year cardiovascular death or hospitalization among patients with 1-month KCCQ-os scores of <25, 25 to <50, 50 to <75, and 75 to 100 was 49%, 32%, 33%, and 21.5%, respectively ($P<0.001$).

After adjustment for ΔKCCQ-os and multiple other patient factors, the relationship between lower 1-month KCCQ scores and all-cause mortality was no longer statistically significant (HR for each 5-point decrease in 1-month KCCQ-os, 1.01; 95% CI, 0.94 to 1.09). The linear relationship between lower 1-month KCCQ-os and combined cardiovascular death and hospitalization, however, persisted (HR for each 5-point decrease in 1 month KCCQ-os, 1.10; 95% CI, 1.05 to 1.16).

TABLE 1. Baseline Characteristics*

Variables	
Demographics	
Age, y	63.5±12
Male, n (%)	1004 (73.9)
White, n (%)	1234 (90.9)
Country, n (%)	
Argentina	82 (6.0)
Belgium	52 (3.8)
Brazil	108 (8.0)
Canada	144 (10.6)
France	45 (3.3)
Germany	240 (17.7)
Netherlands	106 (7.8)
Spain	141 (10.4)
United Kingdom	94 (6.9)
United States	346 (25.5)
Medical comorbidities, n (%)	
Atrial fibrillation	159 (11.7)
Chronic obstructive pulmonary disease	163 (12.0)
Diabetes mellitus	362 (26.7)
Dyslipidemia	790 (58.2)
Stroke or transient ischemic attack	120 (8.8)
Hypertension	764 (56.3)
Cardiovascular disease severity markers on randomization, n (%)	
Prior heart failure	212 (15.6)
Prior angina	586 (43.2)
Prior MI	373 (27.5)
Pulmonary edema	1058 (77.9)
Killip class	
1	249 (18.4)
2	839 (62.1)
3	209 (15.2)
4	57 (4.2)
Post-MI left ventricular ejection fraction, %	32±7
Index event characteristics, n (%)	
Reperfusion attempted (thrombolysis or percutaneous coronary intervention)	822 (60.6)
Baseline clinical parameters†	
Heart rate, bpm	71±12
Systolic blood pressure, mm Hg	118±18
Diastolic blood pressure, mm Hg	71±11
KCCQ-os	70±21
Body mass index, kg/m^2	27±5
Sodium	140±3
Glomerular filtration rate	71±23
Medication use, n (%)	
Angiotensin converting enzyme inhibitors/angiotensin-receptor blockers	1204 (88.7)
β-Blockers	1024 (75.4)
Diuretics	781 (57.5)
Statins	863 (63.5)

n=1358.

*Categorical variables are summarized by frequency and percent. Continuous variables are summarized by mean±SD unless otherwise noted.

†All values represent data at 4 weeks after enrollment.

Predictive Value of 1- to 3-Month ΔKCCQ-os

In unadjusted analysis, a linear relationship existed between ΔKCCQ-os and all-cause mortality (HR for each 5-point decrease in ΔKCCQ-os, 1.11; 95% CI, 1.04 to 1.19). Similarly, ΔKCCQ-os scores also were associated with a higher combined end point of cardiovascular mortality or hospitalization (HR for each 5-point decrease in ΔKCCQ-os, 1.12; 95% CI, 1.07 to 1.18). Adjustment for baseline NYHA class and change in NYHA categories between 1 and 3 months of follow-up had no significant impact on the prognostic importance of ΔKCCQ-os (HR for each 5-point decrease in KCCQ, 1.09 [95% CI, 1.02 to 1.18] for all-cause mortality and 1.10 [95% CI, 1.04 to 1.16] for the combined end point of cardiovascular death or hospitalization). In Kaplan-Meier survival analysis, 2-year all-cause mortality among patients with ΔKCCQ-os of ≤ -10, > -10 to < 10, and > 10 was 26%, 16%, and 13%, respectively ($P=0.008$). Cardiovascular death or hospitalization among patients with 1-month KCCQ-os of ≤ -10, > -10 to < 10, and > 10 was 43%, 24%, and 28%, respectively ($P=0.002$).

After adjustment for 1-month KCCQ-os and multiple other demographic, clinical, disease severity, laboratory, and treatment factors, linear relationships between ΔKCCQ-os and both all-cause mortality and the combined end point of cardiovascular death and hospitalization persisted (for each 5-point decrease in Δ KCCQ-os: HR, 1.09; 95% CI, 1.00 to 1.18; and HR, 1.11; 95% CI, 1.05 to 1.17, respectively). Figure 1A and 1B shows adjusted Kaplan-Meier curves by categories of ΔKCCQ-os. The linear nature (on the log scale) of the relationship between ΔKCCQ-os and the adjusted hazard of all-cause mortality and combined cardiovascular mortality or hospitalization is demonstrated in Figure 2A and 2B.

To demonstrate the reproducibility of the prognostic significance of ΔKCCQ-os, the analysis was replicated using data from the 3- and 6-month visits. The results were nearly identical to the 1- to 3-month ΔKCCQ-os analysis (data not shown). Similarly, the association between 1- to 3-month ΔKCCQ-os and outcomes was not affected by adjustment for 1- to 3-month change in systolic blood pressure, heart rate, and body mass index (for each 5-point decrease in ΔKCCQ-os: HR for all-cause mortality, 1.09; 95% CI, 1.01 to 1.17; and HR for the combined cardiovascular mortality or rehospitalization, 1.10; 95% CI, 1.05 to 1.16). No significant interaction existed between 1-month KCCQ and ΔKCCQ (for the end point of all-cause mortality, P for interaction=0.99; for the end point of cardiovascular mortality or rehospitalization, P for interaction=0.27), suggesting that the effect of ΔKCCQ-os is independent of patients' initial KCCQ-os scores.

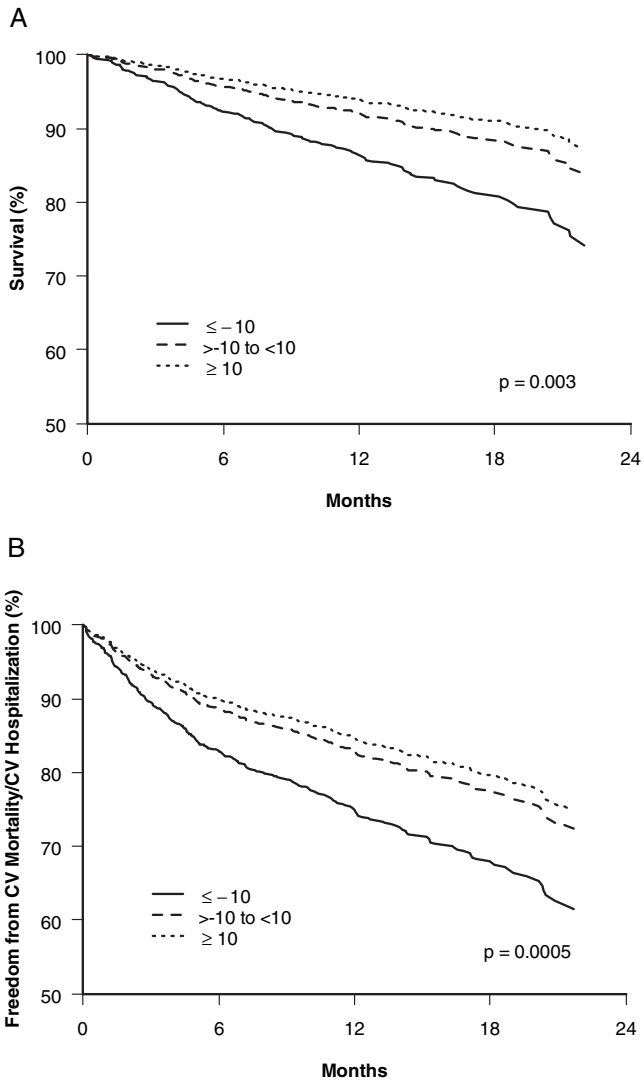

Figure 1. Relationship between 1- to 3-month change in KCCQ-os and all-cause mortality (A) and combined end point of cardiovascular mortality or rehospitalization (B) after multivariable adjustment.

Discussion

Our results demonstrate that serial health status assessment with the KCCQ represents a robust clinical tool for assessing clinical change over time and predicting future adverse events in patients with HF. Change in KCCQ-os had a direct and linear relationship with both all-cause mortality and the combined end point of cardiovascular mortality and hospitalization, even after adjustment (in separate models) for baseline health status score; for change in traditional physician-based assessments of functional status (NYHA class); and for changes in systolic blood pressure, heart rate, and weight, as well as other patient demographic and clinical factors. Our findings suggest that although a single measurement of health status is prognostic, additional valuable prognostic information can be inferred from repeated health status measurements over time. This information can then be used to identify high-risk patients who may warrant a greater frequency of outpatient follow-up and more intense medical or device therapy to optimize their outcomes.

The burden of HF on the healthcare system and the economy is enormous. Despite recent advances in care, HF outcomes remain poor, and hospitalizations related to HF have increased 289% over the past 2 decades,[11] with up to 55% of hospital admissions being potentially preventable.[32–35] For physicians who treat the nearly 5 million patients with HF in the United States,[11] mostly on an outpatient basis, the critical challenge is to effectively identify those patients at risk for subsequent clinical deterioration

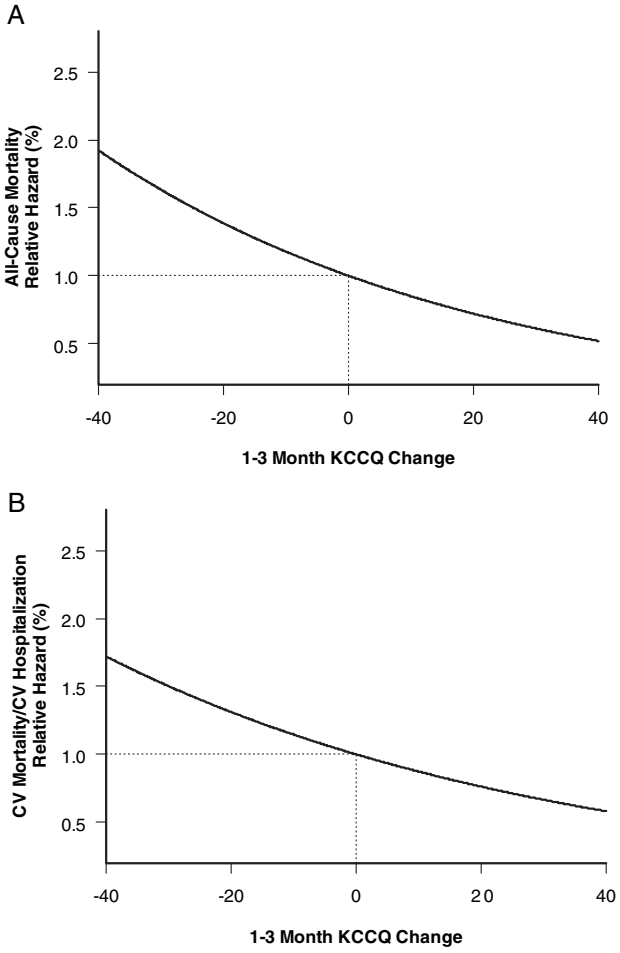

Figure 2. Linear relationship between 1- to 3-month change in KCCQ-os and hazard of all-cause mortality (A) and combined end point of cardiovascular mortality and rehospitalization (B).

so that monitoring and therapy can be intensified and adverse events (including hospitalizations) can be prevented.

Although current American College of Cardiology/American Heart Association (ACC/AHA) guidelines state that an "ongoing review of the patient's clinical status is critical to the appropriate selection and monitoring of treatments,"[22] they provide few tools to assist clinicians in monitoring their patients. Although >80 clinical measures have been proposed for risk stratifying HF patients,[6,36,37] such as echocardiographic,[4,7,9,11,21] electrophysiological,[5,12,19,20] hemodynamic,[13,14,17] biochemical,[3,4,14,16] and exercise/functional determinants,[2–4,7,11,13,15,17] these tend to be invasive, complicated to obtain, and/or costly. Most importantly, their prognostic significance has been determined primarily cross-sectionally, and the association between changes in these measures and patients' prognosis is not known, limiting their ability to be used as tools for longitudinally following up patients over time.

In the present study, we demonstrate that systematic assessment of changes in KCCQ scores using serial measurements in outpatients with HF may indeed be an important tool for monitoring clinical change in HF patients. Because the KCCQ is simple to administer and score, is noninvasive, and can be administered repeatedly at relatively low cost, it may have an important role in clinical management in both individual physician practices and disease management programs in which follow-up and care need to be efficiently provided for entire populations of HF patients. Conceptually, we consider health status assessments with disease-specific, patient-oriented measures such as the KCCQ to represent a formalized history taking. The formal mode of data acquisition offered by the KCCQ, in the form of standardized questions and answers, minimizes the interobserver variability seen in conventional physician-based measures such as the NYHA classification[38] and offers insight into other domains of patient health status that are not sampled by such measures, such as quality of life, self-efficacy, and social limitation. By reproducibly quantifying "how patients are doing" from their perspective, changes can be readily identified and, in light of our findings, interpreted.

Several potential limitations of this study should be noted. First, EPHESUS enrolled only patients with HF after acute MI. Whether changes in KCCQ-os scores have the same prognostic significance in patients with other causes of HF, particularly in those with preserved systolic function, requires future investigation. Second, the overall prognosis of patients in this study was substantially better than previously reported estimates, in which the mortality of HF complicating an MI has been as high as 39%.[39] Although this may reflect the high compliance with guideline-suggested pharmacological treatment, it also is possible that selection bias, as in the avoidance of HF patients with significant renal dysfunction, may have influenced our observed event rate. However, we have no a priori reason to suspect that the relative risk associated with ΔKCCQ-os would vary as a function of HF patients' absolute risk for adverse outcomes. Third, serial health status measurements in our study were administered as a part of routine outpatient follow-up visits within a clinical trial. Whether repeat health status assessments will have similar prognostic value outside this setting (eg, as part of HF disease management programs) remains to be established. Finally, although our results were adjusted for multiple demographic and clinical patient factors, a possibility of residual confounding cannot be definitively excluded. However, the fact that serial assessments of patients' health status can reliably predict clinical deterioration in the future carries a considerable degree of "face validity" from a clinical perspective.

Better strategies are needed to help physicians efficiently target healthcare resources to HF patients at highest risk. Noninvasive risk stratification based on health status instruments such as the KCCQ may be a useful adjunct to current outpatient care. In fact, the ACC/AHA/Physician Consortium for Performance Improvement has advocated the routine documentation of symptoms and function, which includes the use of standardized assessment tools such as the KCCQ, as a marker of high-quality care.[40] The present study facilitates the interpretation of changes in KCCQ scores and supports its use in augmenting the quality of patient care. Future studies are needed to establish whether serial assessment of HF patients with formalized health status assessments such as the KCCQ can improve outcomes.

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Disclosures

Dr Spertus developed and owns the copyrights for the Kansas City Cardiomyopathy Questionnaire, Seattle Angina Questionnaire, and the Peripheral Artery Questionnaire; has leadership responsibilities for CV Outcomes, Inc. and Health Outcomes Sciences and Outcomes Instruments; is a consultant for Amgen, United Healthcare, and Otsuka; receives research grant support from the National Institutes of Health, Amgen, Lilly, Roche Diagnostics, Atherotech, and the American College of Cardiology–National Cardiovascular Data Registry; and previously received grant support from and was a consultant for CV Therapeutics, Inc. Dr Krumholz has research contracts with the Colorado Foundation for Medical Care and the American College of Cardiology; serves on the advisory boards for Amgen, Alere, and United Healthcare; is a subject-matter expert for VHA, Inc; and is editor-in-chief of *Journal Watch Cardiology* of the Massachusetts Medical Society. Dr Weintraub receives grant support from Pfizer. Dr Deedwania has a consulting relationship with Pfizer and receives research grant, speakers' bureau, and honoraria support from Pfizer. The other authors report no conflicts.

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CLINICAL PERSPECTIVE

Few tools are currently available to practicing cardiologists to identify outpatients with heart failure who are at increased risk for clinical deterioration. In this study, we assessed whether serial assessments of patients' health status with the Kansas City Cardiomyopathy Questionnaire (KCCQ) can identify patients at high risk for mortality and hospitalization during outpatient follow-up. We analyzed 1358 patients who developed heart failure after an acute myocardial infarction and had serial health status measurements 1 and 3 months after hospitalization for acute myocardial infraction. We found that deterioration in KCCQ scores was linearly associated with higher risk of death and the combined end point of cardiovascular death or rehospitalization, even after controlling for multiple patient factors, such as measures of disease severity and comorbidities. Importantly, the prognostic impact of change in KCCQ was superior to that of traditional physician-centered health status assessment, specifically, change in the New York Heart Association class. Change in KCCQ score also continued to be predictive of adverse events after adjustment for other commonly used clinical variables such as changes in weight, blood pressure, and heart rate. In summary, serial measurements of health status with KCCQ can identify high-risk outpatients with heart failure and may prove to be useful for directing the frequency of follow-up and the intensity of treatment.