Health Status and Incident Heart Failure in Chronic Kidney Disease

Accumulating Evidence to Use Patient-Reported Measures in Clinical Care

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Chronic kidney disease (CKD) is a strong independent risk factor for several cardiovascular conditions including coronary artery disease, peripheral arterial disease, stroke, and heart failure. Given that the prevalence in the United States is estimated to exceed 10% and is increasing, CKD is an important contributor to persistently high rates of cardiovascular conditions, some of which, like atrial fibrillation and heart failure, have reached epidemic proportions. CKD doubles the risk of developing heart failure independent of concomitant risk factors, such as hypertension and diabetes mellitus. Despite this compelling relationship, CKD, like many other risk factors, is far from a perfect predictor. Further refinements in characterizing the risk of developing clinically overt cardiovascular disease in patients with CKD could therefore be useful.

In a multivariable analysis accounting other measured variables, the KCCQ score was significantly associated with the risk of incident heart failure hospitalization during a mean follow-up of >4 years. In the principal analysis, where the KCCQ was categorized in quartiles, those with the most substantial decrements in health status had a >3-fold odds of an admission for heart failure when compared with the quartile with the best health status (odds ratio, 3.67; P=0.001). This relationship was only slightly attenuated after further adjustment for natriuretic peptide levels and echocardiographic parameters including left ventricular hypertrophy and left ventricular systolic function in the >80% of patients for whom echocardiographic data were available (fully adjusted odds ratio, 3.30; P=0.001). A similar discordance between biological markers and measures of health status has been previously observed in populations with overt heart failure, where despite individual relationships with symptom burden, natriuretic peptide levels and health status measurements using the KCCQ are largely unrelated, and thus reflect independently important constructs.

This study is unique in that it uses a modified version of a widely used instrument to assess symptoms, physical limitation, and quality of life in patients with heart failure and applies it to a population that is at high risk for, but that has not yet experienced, a heart failure event. The findings suggest that modification of a carefully constructed and validated instrument that reflects the patient’s perspective of their well-being may be an important addition to what is ascertained with the medical history.

Beyond the importance of the principal finding, other strengths of the study merit mention. First, the cohort was large and carefully characterized. KCCQ scores were obtained in the vast majority and were measured repeatedly; the analysis thus accounted for fluctuations in the score over time. After identifying hospitalizations from biannual patient interviews and health systems data, the investigators reviewed the medical records and applied the validated Framingham criteria to identify those hospitalizations that were likely to represent heart failure. This rigorous outcome assessment is uncommon in studies of this size. The multivariable models accounted for a wide range of characteristics that might confound the relationship between health status and incident heart failure, including those that might also cause dyspnea or edema as well as natriuretic peptides and measures of cardiac structure and function. Although unmeasured confounding can never be excluded as influencing relationships in observational studies,
the inclusion of these factors supports the independence of the relationship between KCCQ scores and incident heart failure in this patient population.

The study should also be considered in the context of certain limitations. First, among patients with CKD, it may be challenging to distinguish heart failure, which implies some form of cardiac dysfunction, from volume overload. This is presumably particularly true in patients requiring renal replacement therapy. Perhaps not surprisingly, the mean estimated glomerular filtration rate among those in the lowest quartile of KCCQ scores (39.2 mL/min per 1.73 m²) was significantly lower than that in the highest quartile (50.1 mL/min per 1.73 m²). Even the Framingham criteria, which predominantly focus on signs of volume overload on examination and diagnostic tests, cannot specifically implicate cardiac dysfunction as the underlying cause of these findings. It is worth noting, however, that none of the cohort required renal replacement therapy at enrollment, and other reports from the Chronic Renal Insufficiency Cohort found relatively low rates of progression to end-stage renal disease (4.0% during a mean follow-up of 5.4 years).²

Second, the KCCQ, while extensively tested in populations with heart failure,³ was not designed to assess preclinical heart failure as used in this study. From a practical perspective, however, the approach used has face validity as a means of ascertaining otherwise subclinical symptoms of heart failure. The finding that scores on the modified KCCQ predict important health outcomes further supports its use in this context.

Finally, although demonstrating a statistically significant independent relationship between KCCQ scores and heart failure hospitalizations, the study does not measure the extent to which health status assessments improve the classification of patients destined to develop heart failure. As demonstrated by studies of the value of novel biomarkers in predicting cardiovascular events, statistically significant relationships are necessary but not sufficient to demonstrate clinical utility.³ Methods exist to measure the incremental utility of a novel factor, which extend beyond a P value for association.¹⁰ An analysis of the extent to which the KCCQ score reclassifies patients with respect to the risk of heart failure hospitalization would be necessary to understand the degree to which health status could contribute to identifying high-risk patients.

These issues aside, this study adds importantly to the growing literature demonstrating the relevance of patient-reported health status to clinical care. Patient-reported measures of symptoms, physical limitation, and quality of life are intrinsically valuable; their relationship with other outcomes only strengthens the argument for their use. Prior studies in populations with manifest cardiovascular disease have identified important relationships between health status and subsequent outcomes. In patients with heart failure, the KCCQ predicts cardiovascular events, death, and even future costs of care.¹¹–¹³ In patients with coronary artery disease, health status predicts outcomes and healthcare utilization.¹⁴,¹⁵ Further, changes in health status as measured using serial assessments are also predictive independent of baseline values, supporting the value of understanding trajectories of health status over time.¹⁶

Although validated patient-reported measures like the KCCQ are now frequently collected as end points in trials, they have not yet been widely incorporated into clinical care either to facilitate prognostication or to serve as outcomes in their own right. Although the proliferation of technology in medicine, including electronic medical records, personal health records, and telephonic interactive voice response systems, could facilitate the collection and utilization of patient-reported measures, incentives to do so are currently inadequate. This will change. National and international registry programs have begun to incorporate health status measurements.¹⁷,¹⁸ The Centers for Medicare and Medicaid Services is exploring a quality measure for patient-reported outcomes after percutaneous coronary interventions.¹⁹ As such efforts evolve, momentum to integrate health status assessments into the daily activities of clinicians will undoubtedly build.

In the meantime, studies that further enhance our understanding of the use of patient-reported outcomes such as health status should be pursued. Specifically, trials of strategies to act on health status with the objective of improving patients’ well-being and the traditional health outcomes would be useful. Nevertheless, with the knowledge generated by existing data, including the study by Mishra et al, it seems reasonable to contend that the time has come to bring powerful tools that help quantify the impact of disease on symptoms, function, and quality of life into our clinical practice so that we can do better improving the lives of our patients.

Disclosures
Dr Masoudi has a contract with the American College of Cardiology as the Senior Medical Officer of the NCDR.

References


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