Applying the Seattle Heart Failure Model in the Office Setting in the Era of Electronic Medical Records

Brent A. Williams, PhD; Shikhar Agarwal, MD

**Background:** Prediction models such as the Seattle Heart Failure Model (SHFM) can help guide management of heart failure (HF) patients, but the SHFM has not been validated in the office environment. This retrospective cohort study assessed the predictive performance of the SHFM among patients with new or pre-existing HF in the context of an office visit.

**Methods and Results:** SHFM elements were ascertained through electronic medical records at an office visit. The primary outcome was all-cause mortality. A "warranty period" for the baseline SHFM risk estimate was sought by examining predictive performance over time through a series of landmark analyses. Discrimination and calibration were estimated according to the proposed warranty period. Low- and high-risk thresholds were proposed based on the distribution of SHFM estimates. Among 26,851 HF patients, 14,380 (54%) died over a mean 4.7-year follow-up period. The SHFM lost predictive performance over time, with C=0.69 and C<0.65 within 3 and beyond 12 months from baseline respectively. The diminishing predictive value was attributed to modifiable SHFM elements. Discrimination (C=0.66) and calibration for 12-month mortality were acceptable. A low-risk threshold of ~5% mortality risk within 12 months reflects the 10% of HF patients in the office setting with the lowest risk.

**Conclusions:** The SHFM has utility in the office environment.

**Key Words:** Heart failure; Prognosis; Risk assessment

Despite therapeutic advances, heart failure (HF) remains an extremely morbid condition associated with frequent distressing symptoms and a 5-year mortality rate approaching 50% following diagnosis. Although aggregate experience informs the expected clinical trajectory, the subsequent clinical course of any single HF patient is difficult to predict, particularly in the office setting, where patients are more likely to be relatively stable and have no obvious signals serving as impetus to alter care. Prognosis estimation can help guide the management of such patients, yet relying solely on clinical intuition for such a task can be challenging. To make prognosis estimation more objective, several risk prediction models have been developed that transform a collection of prognostic determinants into a single numeric estimate of absolute mortality risk over a specified time frame. Risk prediction models enable better placement of individuals along the risk continuum, allowing, in theory, more judicious and cost-efficient application of HF therapies. Furthermore, electronic medical record (EMR) systems should make such models easier to apply in the future by serving as a repository for necessary data elements, providing an environment for behind-the-scenes calculations of quantitative risk estimates, and displaying quantitative model output with accompanying management recommendations as a form of clinical decision support.

The Seattle Heart Failure Model (SHFM) is arguably the most popular and well-validated HF prognostic model. Although developed in a small, clinical trial cohort limited to HF patients with an ejection fraction (EF) <35% and New York Heart Association (NYHA) Class III or IV, the SHFM has been externally validated in both more and less healthy HF cohorts with variable predictive performance. However, to our knowledge, the SHFM has not been validated among HF patients in the context of the office visit. The transportability of the SHFM to the office setting is questionable given large discrepancies in disease severity between the SHFM derivation cohort and HF patients in the office environment. Accordingly, in the present study we assessed several predictive properties of the SHFM in the office environment to evaluate its potential utility in this common setting. In addition to common metrics of predictive performance, such as discrimination and calibration, we also sought to determine the “warranty period” of a baseline risk estimate from the SHFM. Because several of the SHFM elements reflect transient, modifiable states, we hypothesized that the predictive value of a single baseline risk estimate would wane over time. Finally, risk thresholds are proposed for labeling HF patients as low and high risk in the office setting.
Methods

Geisinger Health System Patient Population

The present retrospective cohort study incorporated the patient population and EMR data repository of the Geisinger Health System (Geisinger). Study inclusion criteria were designed to identify patients with an established HF diagnosis at the time of an office visit with maximum availability of SHFM elements. Specifically, inclusion criteria consisted of: (1) having received primary care and other healthcare services through Geisinger for at least a 2-year period; and (2) having a pre-existing or new diagnosis of HF as defined by the presence of the appropriate International Classification of Diseases – Ninth Revision (ICD-9) codes observed as a primary or secondary diagnosis at either 1 inpatient or 2 separate outpatient encounters. A baseline date was defined as the date of the first Geisinger office visit after inclusion criteria were met. The ≥2-year pre-office visit time interval was used to establish patient characteristics as of the baseline date. All patients meeting inclusion criteria with a baseline date between 1 January 2003 and 31 December 2014 were considered. All-cause mortality was obtained through the EMR with follow-up through 19 August 2015 (the date of study approval by the Geisinger Institutional Review Board [IRB]). The Geisinger IRB granted a waiver of patient consent given the retrospective nature of the study. Patients not known to have died were censored at their last Geisinger encounter prior to the study termination date.

SHFM Elements

All SHFM elements were determined with reference to the aforementioned baseline date. The present study focuses on the original 14-element SHFM consisting of age, gender, NYHA functional class, EF, ischemic etiology of HF, systolic blood pressure (SBP), statin use, allopurinol use, diuretic dose (adjusted for body weight), hemoglobin, percentage of white blood cells in the form of lymphocytes, uric acid; in addition, sodium, cholesterol, and potassium were also included as modifiable elements. Specifically, inclusion criteria were designed to identify patients with an established HF diagnosis at the time of an office visit with maximum availability of SHFM elements. Specifically, inclusion criteria consisted of: (1) having received primary care and other healthcare services through Geisinger for at least a 2-year period; and (2) having a pre-existing or new diagnosis of HF as defined by the presence of the appropriate International Classification of Diseases – Ninth Revision (ICD-9) codes observed as a primary or secondary diagnosis at either 1 inpatient or 2 separate outpatient encounters. A baseline date was defined as the date of the first Geisinger office visit after inclusion criteria were met. The ≥2-year pre-office visit time interval was used to establish patient characteristics as of the baseline date. All patients meeting inclusion criteria with a baseline date between 1 January 2003 and 31 December 2014 were considered. All-cause mortality was obtained through the EMR with follow-up through 19 August 2015 (the date of study approval by the Geisinger Institutional Review Board [IRB]). The Geisinger IRB granted a waiver of patient consent given the retrospective nature of the study. Patients not known to have died were censored at their last Geisinger encounter prior to the study termination date.

Analytic Strategy

The first analytic goal was to determine the “warranty period” of a single baseline risk estimate calculated from the SHFM. The rationale for this analysis is that several elements of the SHFM reflect transient, modifiable states that should demonstrate stronger predictive performance shortly after baseline, with progressively worsening performance as time from baseline increases. The proposed warranty period is that post-baseline time point beyond which the predictive information provided by the SHFM is deemed unacceptably poor, and thus serves as a recommended maximum time point by which risk estimates should be recalculated. Multiple potential warranty periods were quantitatively assessed through a series of landmark analyses in which post-baseline follow-up time was divided into 20 non-overlapping 3-month intervals up to 5 years following baseline. Patients were included in any 3-month interval when they were known to be alive and not lost to follow-up at the end of the preceding interval. The C-statistic as appropriate for censored data was calculated for each 3-month interval using the linear predictor (LP) from the SHFM assessed at baseline as the sole predictor variable. The LP is the sum of the products of the SHFM regression coefficients as reported by Levy et al and the values (x) of the 14 model elements assigned at baseline, as follows:

\[ LP = \beta_{age} \times x_{age} + \beta_{male} \times x_{male} + \ldots + \beta_{uric} \times x_{uric} = 2\beta x \]

Estimated per-individual survival according to the SHFM at any time point t (in years) is determined by the following formula:

\[ S(t) = (e^{-0.0405t})^{\text{LP}} \]

Thus, estimated mortality at time t is 1−S(t).

Interval-specific C-statistics from the series of landmark analyses were plotted by 3-month intervals over time to assess the decrement in predictive performance of the baseline SHFM risk estimate over time. The modifiable and non-modifiable elements of the LP were evaluated separately with partial C-statistics that only consider the coefficient-covariate pairs from the LP related to the modifiable and non-modifiable elements respectively. The modifiable elements were expected to show a greater decrement in predictive performance over time than the non-modifiable elements. The 9 modifiable elements were EF, SBP, diuretic dose, NYHA class, sodium, cholesterol, hemoglobin, percentage lymphocytes, and uric acid; in contrast, the 5 non-modifiable elements were age, gender, ischemic etiology, statin use, and allopurinol use. Similar partial C-statistic plots were generated for each of the 14
Applying the SHFM at an Office Visit

Thresholds for “low” and “high” risk were proposed based on percentiles of the distribution of 12-month mortality estimates as calculated from the SHFM. Sensitivity analyses were performed that repeated these analyses after separating patients into preserved (≥50%) and reduced (<50%) EF.

Results

Among 1,160,591 patients with at least 1 encounter at Geisinger between 1 January 2001 and 31 December 2014, 430,913 met the primary care and ≥2 years between first and last encounters criteria stated above. In all, 26,851 HF patients met all study inclusion criteria, and 14,380 (54%) were known to have died by the end of the study period. Mean (±SD) follow-up among known survivors was 4.7 ± 3.7 years. Geisinger HF patients were older than patients from individual SHFM elements. An acceptable warranty period for the baseline SHFM risk estimate was determined subjectively through visual inspection of the plots.

Estimates of discrimination and calibration of the SHFM were based on the proposed warranty period (i.e., 12-month mortality). Discrimination, the degree of concordance between the baseline LP (estimated risk) and survival times, was determined by the C-statistic for censored data with follow-up truncated at 12 months. Calibration was evaluated as the extent of agreement between expected 12-month mortality as estimated by the SHFM and observed 12-month mortality among Geisinger patients as estimated by the Kaplan-Meier (KM) method. A calibration plot was created where estimated and observed 12-month mortality rates were compared within strata of estimated mortality. Strata were created for every 1% increment in estimated mortality from <3%, 3–<4%, 4–<5%, ..., 29–<30%, and ≥30%. Thresholds for “low” and “high” risk were proposed based on percentiles of the distribution of 12-month mortality estimates as calculated from the SHFM. Sensitivity analyses were performed that repeated these analyses after separating patients into preserved (≥50%) and reduced (<50%) EF.

Table 1. Elements of the SHFM: Geisinger HF Patients and SHFM Derivation Set Patients

| SHFM element | Geisinger HF patients (n=26,851) | SHFM derivation set (n=1,125) |
|-------------|---------------------------------|-------------------------------|
| Age (years) | 73±13                           | 65±11                         |
| Male (%)    | 50                              | 76                            |
| NYHA class  | NA                              | 3.6                           |
| EF (%)      | 50±15 (n=7,978, 30% missing)    | 21±6                          |
| Ischemic etiology (%) | 49                             | 64                            |
| SBP (mmHg)  | 129±20 (n=190, <1% missing)     | 118±18                        |
| Diuretic dose (mg/kg) | 0.67±0.81                      | 1.45±1.33                     |
| Allopurinol (%) | 8                              | 10                            |
| Statin (%)  | 58                              | 8                             |
| Sodium (mEq/L) | 139±3 (n=2,187, 8% missing)    | 139±4                         |
| Cholesterol (mg/dL) | 176±44 (n=7,518, 28% missing) | 202±50                        |
| Hemoglobin (g/dL) | 12.9±1.9 (n=3,441, 13% missing) | 13.9±1.7                     |
| % Lymphocytes | 22±10 (n=8,186, 30% missing)   | 26±9                          |
| Uric acid (mg/dL) | 7.0±2.3 (n=23,200, 86% missing) | 8.9±2.6                     |

Unless indicated otherwise, data are given as the mean±SD. Includes only non-missing values. EF, ejection fraction; HF, heart failure; NYHA, New York Heart Association; SBP, systolic blood pressure; SHFM, Seattle Heart Failure Model.

Table 2. Seattle HF Model Elements Among Geisinger HF Patients Stratified by Reduced vs. Preserved EF

| Model element | Reduced EF (n=7,397) | Preserved EF (n=11,476) | Missing EF (n=7,978) |
|--------------|----------------------|-------------------------|----------------------|
| Age (years)  | 70±13                | 73±13                   | 75±13                |
| Male (%)     | 64                   | 44                      | 46                   |
| NYHA class   | NA                   | NA                      | NA                   |
| EF (%)       | 34±9                 | 60±7                    | NA                   |
| Ischemic etiology (%) | 65               | 44                      | 40                   |
| SBP (mmHg)   | 125±20               | 131±20                  | 131±20               |
| Diuretic dose (mg/kg) | 0.70±0.83           | 0.70±0.81               | 0.60±0.79            |
| Allopurinol (%) | 8                   | 8                       | 7                    |
| Statin (%)   | 68                   | 59                      | 46                   |
| Sodium (mEq/L) | 139±3               | 139±3                   | 139±3               |
| Cholesterol (mg/dL) | 173±46             | 175±44                  | 180±44               |
| Hemoglobin (g/dL) | 13.1±2.0           | 12.7±1.9                | 13±1.9               |
| % Lymphocytes | 21±10               | 22±10                   | 22±10                |
| Uric acid (mg/dL) | 7.0±2.3            | 6.9±2.3                 | 7.2±2.4             |

Unless indicated otherwise, data are given as the mean±SD. Includes only non-missing values. Abbreviations as in Table 1.
Observed survival as derived by the KM method was 87%, 68%, 53%, and 26% at 1, 3, 5, and 10 years following baseline, respectively, whereas the SHFM-based estimated survival at these time points was 87%, 68%, 54%, and 32%, respectively. Assuming different average NYHA classes other than 2.5 led to either mild underestimation (NYHA=2) or overestimation (NYHA=3) of expected mortality from the SHFM (data not shown).

Within each 3-month interval following baseline, approximately 3% of patients alive at the beginning of each interval died by the end of the interval, and at least 295 deaths occurred within each interval up to 5 years following baseline (Table S1). The baseline risk estimate (LP) from the SHFM showed decreasing predictive performance over time since baseline, as shown by decreasing interval-specific C-statistics over the course of follow-up (Figure 2). The C-statistic was 0.69 within 3 months of baseline, and decreased steadily up to 36 months following baseline with C-statistics near 0.60. As expected, a similar pattern was observed when restricting to the modifiable elements of the SHFM, whereas the non-modifiable elements showed poor predictive performance in the early period after baseline with no discernable pattern beyond 12 months (Figure 2). Examining trends for the individual modifiable elements revealed that the predictive performance of hemoglobin, sodium, SBP, and EF decreased sharply over the follow-up period, whereas diuretic dose and percentage lymphocytes largely retained their predictive value up to 15 months beyond baseline (Figure 3). Similar plots for the non-modifiable components showed no discernable patterns (Figure 4). Based on visual inspection of these plots, subsequent analyses were restricted to 12-month mortality, the proposed “warranty period”. The C-statistic for 12-month mortality was 0.66, and was similar among patients with both preserved (C=0.65) and reduced (C=0.66) EF.

Although overall agreement between expected (from the SHFM) and observed 12-month mortality was strong...
Applying the SHFM at an Office Visit

The primary goal of the present study was to assess the predictive performance of the SHFM when applied to HF patients at an office visit and provide practical guidance to practitioners seeking to use the SHFM longitudinally to inform clinical decisions. The present study demonstrates \((\text{Figure 1})\), the SHFM tended to overestimate risk in lower-risk patients (maximum absolute deviation +1.6%) and underestimate risk in higher-risk patients (maximum absolute deviation −5.2%; \text{Figure 5}). The calibration patterns were not noticeably different among patients with preserved and reduced EF. The 10th percentile of SHFM 12-month mortality estimates (“low risk”), representing the 10% lowest-risk HF patients in the office setting, was 5.8% (Table 2). Conversely, the 90th percentile of estimates (“high risk”) was 21.6% (Table 3). Other percentiles of the distribution of 12-month mortality estimates from the SHFM are given in Table 3.

\textbf{Discussion}

The primary goal of the present study was to assess the predictive performance of the SHFM when applied to HF patients at an office visit and provide practical guidance to practitioners seeking to use the SHFM longitudinally to inform clinical decisions. The present study demonstrates...
suggested as ~5% mortality risk in the next 12 months, and, given the abundance of modifiable components in the SHFM, could serve as a therapeutic target evaluated longitudinally through repeat assessment of 12-month mortality risk according to the SHFM.

Although the SHFM is arguably the most popular and well-validated HF prognostic model for objectively differentiating risk, its transportability to the office environment should be questioned given the large discrepancy in case-mix between the clinical trial-derived SHFM derivation set and HF patients managed in the office setting. Indeed, the present study patients derived from a primary care population at an office visit were older, had a more balanced male:female distribution, higher EF, and required lower diuretic doses than the trial-derived SHFM patients. These differences may have contributed to the relatively modest predictive performance of the SHFM in our patients. The C-statistic for 12-month mortality was just 0.66 in the present study, in contrast with the 0.72 observed in the SHFM derivation set. However, the SHFM showed strong calibration in the office environment (Figures 1, 5), suggesting SHFM estimates can be applied to HF patients in the office setting without the need for adjustment (recalibration). Importantly, the discrimination and calibration of the SHFM were not appreciably different among patients with preserved vs. reduced EF, an important observation considering the SHFM was initially developed among patients with EF <35%. Thus, in the office environment, the SHFM provided consistent predictive information regardless of EF.

Using the SHFM
A key practical objective of using HF prognostic models is better placement of individuals along the risk continuum such that efficacious yet cost-efficient therapeutic measures can be applied appropriately across the entire risk spectrum. Indeed, there is a prevailing wisdom that higher-risk patients warrant more aggressive therapy via increased

| Percentile   | 12-month mortality estimate (%) |
|--------------|---------------------------------|
| 5th          | 4.9                             |
| 10th         | 5.8                             |
| 20th         | 7.2                             |
| 25th (1st quartile) | 7.8                         |
| 30th         | 8.4                             |
| 40th         | 9.5                             |
| 50th (median)| 10.8                            |
| 60th         | 12.3                            |
| 70th         | 14.2                            |
| 75th (3rd quartile) | 15.4                        |
| 80th         | 16.9                            |
| 90th         | 21.6                            |
| 95th         | 26.8                            |
Applying the SHFM at an Office Visit

In contrast, lower-risk patients can often be treated less aggressively given the lower expected benefit and unjustified risk of side effects. To our knowledge, no thresholds for low or high mortality risk have been suggested that can be applied to HF patients in the context of an office visit. Our proposed low- and high-risk thresholds (−5% and −20% 12-month mortality risk, respectively) are based on the 10th and 90th percentiles of the distribution of SHFM risk estimates, reflecting the healthiest and sickest 10% of HF patients according to SHFM risk factor status at the time of an office visit. Although these suggested thresholds warrant validation, the low-risk threshold could possibly serve as a therapeutic target via dynamic risk assessment, whereas exceeding the high-risk threshold could warrant consideration of more aggressive therapeutic measures to lower risk.

Dynamic Risk Assessment Using the SHFM

The declining predictive value of a 1-time, baseline risk estimate from the SHFM suggests regular updating of modifiable model elements should be recommended for optimal clinical incorporation of model results. Indeed, the results of the present study show that the predictive value of a baseline SHFM risk estimate decreases in a relatively consistent manner, with the 3-month interval-specific C-statistics reaching a nadir around 36 months after baseline. Investigation of individual modifiable elements suggests the declining predictive performance is mostly attributed to baseline measurements of hemoglobin, sodium, SBP, and EF. Previous studies have shown the temporally declining predictive performance of the SHFM and other HF prognostic models, and certain individual modifiable prognostic factors as time since risk assessment increases. For example, Sartipy et al., using the SHFM, showed that C-statistics decreased from 0.774 to 0.742 to 0.728 at 1, 2, and 3 years following assessment. These decrements in predictive performance are not unexpected because a 1-time measurement of a modifiable element may characterize only a transient, correctable state whose status may change with disease progression and treatment alterations. Accordingly, several studies have observed that updated values of modifiable components provide better prognostic information than preceding values. This phenomenon suggests that continually updating modifiable components provides improved prognostic information beyond a single baseline assessment. Indeed, the potential value of repeated (dynamic) risk assessment with the SHFM (or any prognostic model with modifiable components) lies in the collective ability of the modifiable elements to quantify relevant, HF-induced pathophysiologic processes that could serve as a gauge of disease progression and/or therapeutic effectiveness. An intriguing although untested hypothesis is whether clinical management of HF patients guided by a dynamic risk measure (with a goal of minimizing the risk measure) may be a more efficient and efficacious method for minimizing untoward events relative to standard of care. This strategy has analogy with, but extends, an extensive collection of work using natriuretic peptides as a dynamic risk marker for guiding treatment decisions.

Clinical Implementation of the Seattle HF Model

Although difficult to verify, application of HF prognostic models in clinical practice does not appear widely prevalent, despite some evidence suggesting that objective mathematical prediction models may allow better predictions in certain scenarios than physician intuition. Certain barriers to model implementation have been identified, particularly the challenge of performing calculations in a busy clinical environment, difficulty for clinicians and patients in interpreting probabilistic model output, especially when not accompanied by actionable advice, and the limited accuracy of prediction models, due, in part, to the omission of important prognostic factors unaccounted for by the model but available to the treating clinician to enhance their subjective judgement. Although the SHFM developers have created an Internet-based tool for facilitating calculation of risk estimates, physician use of prediction models like the SHFM likely requires that the model regularly provides information not otherwise available for clinical decision making (e.g., scenarios where a high-risk state is created not by a gross abnormality of a single risk factor, but rather several mild abnormalities acting collectively to portend high risk). Furthermore, going through the calculation process may draw attention to an aberrant value of a lesser appreciated prognostic factor that may be amenable to modification (e.g., low cholesterol). Finally, as discussed above, the SHFM can be applied repeatedly at future time points whenever new information on model elements becomes available as a means to track risk, monitor disease progression, and assess therapeutic effectiveness.

Study Limitations

Some limitations of the present study should be noted. The present study relied on EMRs for gathering SHFM elements, thus study validity is partially dependent on the quality of medical record documentation. Although measurement error and missing data are concerns, the present study likely reflects the quality and quantity of data that would be available in the typical office setting where the SHFM would be applied. Importantly, the predictive performance of the SHFM was not sensitive to the number of missing elements (median of 3); this is likely explained by uncommon missing values for the strongest predictive elements, including current diuretic dose, SBP, and hemoglobin. Certain variables that are capable of being defined more precisely at an actual office visit could only be defined imprecisely in the present retrospective study. These study attributes likely caused attenuation of predictive performance metrics. Several HF prognostic models have been developed, but the SHFM was selected because it is arguably the most popular, even receiving mention in HF guidelines. No model is comprehensive in including all important predictors of HF mortality, and the SHFM is especially notable for its exclusion of natriuretic peptides. Importantly, numerous other modifiable biomarkers with greater cardiac specificity are receiving increased attention as prognostic factors. We intentionally chose the office visit setting as the initial assessment point in an attempt to capture HF patients at a relatively stable phase of their disease, but we cannot exclude that some office visits were instigated as a response to early decompensation.

Conclusions

In conclusion, the present analysis suggests that the SHFM may have utility in the office environment. The
discrimination of the SHF-M was decent within 12 months of its assessment, but predictive performance was suboptimal beyond 12 months, suggesting that at least annual repeat measurements of modifiable elements allows better application of the model. Calibration was generally good across the spectrum of SHF-M-estimated risk. A 5% risk of 12-month mortality may be a reasonable low-risk threshold that could serve as a therapeutic target via dynamic risk assessment.

**Source of Funding**

This investigator-initiated study was funded by Roche.

**Conflict of Interest**

B.A.W. has received other research funding from Biosense Webster, Daichi Sankyo, Boehringer Ingelheim, Gilead, Merck, Edwards Lifesciences, and Janssen. S.A. reports no conflicts of interest.

**References**

1. Liu L, Eisen HJ. Epidemiology of heart failure and scope of the problem. *Cardiol Clin* 2014; 32: 1–8.
2. Braunwald E. Heart failure. *J Am Coll Cardiol HF* 2013; 1: 1–20.
3. Roger VL. Epidemiology of heart failure. *Circ Res* 2013; 113: 646–659.
4. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure. *J Am Coll Cardiol* 2013; 62: e147–e239.
5. Owens AT, Brozena SC, Jessup M. New management strategies in heart failure. *Circ Res* 2016; 118: 480–495.
6. Alba AC, Agoritsas T, Jankowski M, Courvoisier D, Walter SD, Guyatt GH, et al. Risk prediction models for mortality in ambulatory patients with heart failure: A systematic review. *Circ Heart Fail* 2013; 6: 881–889.
7. Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, et al. Forecasting the impact of heart failure in the United States: A policy statement from the American Heart Association. *Circ Heart Fail* 2013; 6: 606–619.
8. Allen LA, Stevenson LW, Grady KL, Goldstein NE, Matlock DD, Arnold RM, et al. Decision making in advanced heart failure: A scientific statement from the American Heart Association. *Circulation* 2012; 125: 1928–1952.
9. Ferrero P, Iacovoni A, D’Elia E, Vaduganathan M, Gavazzi A, Senni M. Prognostic scores in heart failure: Critical appraisal and practical use. *Int J Cardiol* 2015; 188: 1–9.
10. Prognostic research. In: Grobbee DE, Hoes AW, editors. Clinical epidemiology, 2nd edn. Burlington, MA, USA: Jones & Bartlett Learning, 2015; 117–150.
11. Moons KG, Kengne AP, Woodward M, Royston P, Vergouwe Y, Altman DG, et al. Risk prediction models: I. Development, internal validation, and assessing the incremental value of a new (bio)marker. *Heart* 2012; 98: 683–690.
12. Levy WC, Mozaffarian D, Linker DT, Sutrathdar SC, Anker SD, Cropp AB, et al. The Seattle Heart Failure Model: Prediction of survival in heart failure. *Circulation* 2006; 113: 1424–1433.
13. Aaronson KD, Cowger J. Heart failure prognostic models: Why bother? *Circ Heart Fail* 2012; 5: 6–9.
14. Shiraiishi Y, Sawano M, Kohno T, Nishiyama T, Maekawa Y, Sano M, et al. Validation of the Seattle Heart Failure Model in Japanese heart failure patients. *Int J Cardiol* 2016; 203: 87–89.
15. Vakil KP, Roukouz H, Tung R, Levy WC, Anand IS, Shivkumar K, et al. Mortality prediction using a modified Seattle Heart Failure Model may improve patient selection for ventricular tachycardia ablation. *Am Heart J* 2015; 170: 1099–1104.
16. Sartipy U, Goda A, Yuzepolskaya M, Mancini DM, Lund LH. Utility of the Seattle Heart Failure Model in patients with cardiac resynchronization therapy and implantable cardioverter defibrillator referred for heart transplantation. *Am Heart J* 2014; 168: 325–331.
17. Stefanescu A, Macklin EA, Lin E, Dudzinski DM, Johnson J, Kennedy KF, et al. Usefulness of the Seattle Heart Failure Model to identify adults with congenital heart disease at high risk of poor outcome. *J Am Coll Cardiol* 2014; 63: 865–870.
18. Kalogeropoulos AP, Georgiopoulou VV, Giamouzis G, Smith AL, Agha SA, Waheed S, et al. Utility of the Seattle Heart Failure Model in patients with advanced heart failure. *J Am Coll Cardiol* 2009; 53: 334–342.
19. May HT, Horne BD, Levy WC, Kfouri AG, Rasmusson KD, Linker DT, et al. Validation of the Seattle Heart Failure Model in a community-based heart failure population and enhancement by adding B-type natriuretic peptide. *Am J Cardiol* 2007; 100: 697–700.
20. Williams BA, Doddamani S, Troup MA, Mowery AL, Klime CM, Gerringer JA, et al. Agreement between heart failure patients and providers in assessing New York Heart Association functional class. *Heart Lung* 2017; 46: 293–299.
21. Putter H. Landmarking. In: Klein JP, van Houwelingen HC, Ibrahim JG, Scheike TH, editors. Handbook of survival analysis. Boca Raton, FL, USA: Chapman & Hall, 2014; 441–456.
22. Evaluation of performance. In: Steyerberg EW, editor. Clinical prediction models. New York, NY, USA: Springer, 2009; 255–280.
23. Moons KG, Kengne AP, Grobbee DE, Royston P, Vergouwe Y, Altman DG, et al. Risk prediction models: II. External validation, model updating, and impact assessment. *Heart* 2012; 98: 691–698.
24. Thorvaldsen T, Benson L, Ståhlberg M, Dahlström U, Edner M, Lund LH. Triage of patients with moderate to severe heart failure: Who should be referred to a heart failure center? *J Am Coll Cardiol* 2014; 63: 661–671.
25. Agostini P, Corrà U, Cattadori G, Veglia F, La Gioia R, Scardovi AB, et al. Metabolic exercise test data combined with cardiac and kidney indexes, the MECKI score: A multiparametric approach to heart failure prognosis. *Int J Cardiol* 2013; 167: 2710–2718.
26. Alehagen U, Dahlström U, Rehfeld JF, Goetze JP. Pro-A-type natriuretic peptide, proadrenomedullin, and N-terminal pro-B-type natriuretic peptide used in a multimarker strategy in primary health care in risk assessment of patients with symptoms of heart failure. *J Card Fail* 2013; 19: 31–39.
27. Troughton R, Felker GM, Januzzi JL. Natriuretic peptide-guided heart failure management. *Eur Heart J* 2014; 35: 16–24.
28. Januzzi JL, Troughton R. Serial natriuretic peptide measurements are useful in heart failure management. *Circulation* 2013; 127: 500–508.
29. Miller WL, Grill DE, Struck J, Jaffe AS. Association of hyponatremia and elevated copeptin with death and need for transplantation in ambulatory patients with chronic heart failure. *Am J Cardiol* 2013; 111: 880–885.
30. Motiwala SR, Januzzi JL. Using biomarkers to “guide” heart failure management: Current perspectives and future directions. *Circ Res* 2013; 112: 127–134.
31. Licata M, Rossi A, Chiampi A, Frigo G, Bergamini C, Rigoli M, et al. Identification of high-risk chronic heart failure patients in clinical practice: Role of changes in left ventricular function. *Clin Cardiol* 2012; 35: 580–584.
32. Kappen TH, van Loon K, Kappen MA, van Wolfswinkel K, Vergouwe Y, van Klei WA, et al. Barriers and facilitators perceived by physicians when using prediction models in practice. *J Clin Epidemiol* 2016; 70: 136–145.
33. Howlett JG. Should we perform a heart failure risk score? *Circ Heart Fail* 2013; 6: 4–5.
34. Braunwald E. Research advances in heart failure. *Comp Circ* 2013; 113: 633–645.

**Supplementary Files**

**Supplementary File 1**

| Table S1. | Total number of patients at risk at the beginning of the 3-month intervals, and the number of deaths within the 3-month intervals |
|----------|-------------------------------------------------------------------------------------------------|
| Please find supplementary file(s): | http://dx.doi.org/10.1253/circ.CJ-17-0670 |